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(54) Title: PROTEIN KINASES

(57) Abstract: The present invention relates to novel kinase polypeptides, nucleotide sequences encoding the novel kinase polypep-  
tides, as well as various products and methods useful for the diagnosis and treatment of various kinase-related diseases and conditions.

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DESCRIPTION  
PROTEIN KINASES

FIELD OF THE INVENTION

5           The present invention relates to novel kinase polypeptides, nucleotide sequences encoding the novel kinase polypeptides, as well as various products and methods useful for the diagnosis and treatment of various kinase-related diseases and conditions.

BACKGROUND OF THE INVENTION

10           The following description of the background of the invention is provided to aid in understanding the invention, but is not admitted to be or to describe prior art to the invention.

15           Cellular signal transduction is a fundamental mechanism whereby external stimuli that regulate diverse cellular processes are relayed to the interior of cells. One of the key biochemical mechanisms of signal transduction involves the reversible phosphorylation of proteins, which enables regulation of the activity of mature proteins by altering their structure and function.

20           Protein phosphorylation plays a pivotal role in biological signal transduction. Among the biological functions controlled by protein phosphorylation are the following: cell division; differentiation and death (apoptosis); cell motility and cytoskeletal structure; control of DNA replication, transcription, splicing and translation; protein translocation events from the endoplasmic reticulum and Golgi apparatus to the membrane and extracellular space; protein nuclear import and export; regulation of metabolic reactions, etc. Abnormal protein phosphorylation is widely recognized to be causally linked to the etiology of many diseases including cancer as well as immunologic, neuronal and metabolic disorders.

25           The most common phospho-acceptor amino acid residues are serine, threonine and tyrosine. Phosphorylation in histidine has also been observed in bacteria. The presence of a phosphate moiety modulates protein function in multiple ways. A common mechanism includes changes in the catalytic properties ( $V_{max}$  and  $K_m$ ) of an enzyme leading to its activation or inactivation. A second widely recognized mechanism involves promoting protein-protein interactions. An example of this is the tyrosine autophosphorylation of the

30



ligand-activated EGF receptor tyrosine kinase. This event triggers the high-affinity binding to the phosphotyrosine residue on the receptor's C-terminal intracellular domain to the SH2 motif of the adaptor molecule Grb2. Grb2 in turn binds through its SH3 motif to a second adaptor molecule, such as SHC. The formation of this ternary complex activates the signaling events that are responsible for the biological effects of EGF. Serine and threonine phosphorylation events have also been recently recognized to exert their biological function through protein-protein interaction events mediated by the high-affinity binding of phosphoserine and phosphothreonine to WW motifs present in a large variety of proteins (Lu, P.J. *et al.* (1999) *Science* 283:1325-1328). A third important outcome of protein phosphorylation is changes in the subcellular localization of the substrate. As an example, nuclear import and export events in a large diversity of proteins are regulated by protein phosphorylation (Drier E.A. *et al.* (1999) *Genes Dev* 13: 556-568).

Protein kinases are one of the largest families of eukaryotic proteins with several hundred known members. These proteins share a 250-300 amino acid domain that can be subdivided into 12 distinct subdomains that comprise the common catalytic core structure. These conserved protein motifs have recently been exploited using PCR-based and bioinformatic strategies leading to a significant expansion of the known kinases. Multiple alignment of the sequences in the catalytic domain of protein kinases and subsequent parsimony analysis permits their segregation into a dendrogram reflecting the relatedness of their catalytic domains (Fig. 1). In this manner, related kinases are clustered into distinct branches or subfamilies including: tyrosine kinases, cyclic-nucleotide-dependent kinases, calcium/calmodulin kinases, cyclin-dependent kinases and MAP-kinases, serine-threonine kinase receptors, and several other less defined subfamilies.

We have recently completed a systematic analysis of the protein kinases present in *C. elegans*, the multicellular organism whose entire DNA sequence has been determined. We identified 473 unique kinase profiles including 398 full-length conventional kinases, and 20 additional proteins that may function as atypical protein kinases. (Plowman G.D. *et al.* (1999), *Proc. Natl. Acad. Sci.* 96:13603-13610).

Using parsimony analysis, the protein kinases may be divided into 4 major groups: AGC, CAMK, CMGC and tyrosine kinases. In addition, there are a number of minor yet distinct families, including the STE and casein kinase 1, families related to worm- or

fungus-specific kinases, and a family designated "other" to represent several smaller families. In addition, we designate an "atypical" family to represent protein kinases whose catalytic domain has little or no primary sequence homology to conventional kinases, including the A6 kinases and PI3 kinases.

5       The AGC kinases are basic amino acid-directed enzymes that phosphorylate residues found proximal to Arg and Lys. Examples of this group are the cyclic nucleotide-dependent kinases, G protein kinases, NDR or DBF2 and the ribosomal S6 kinases.

10       The CAMK group kinases are also basic amino acid-directed kinases. They include the Ca<sup>2+</sup>/calmodulin-regulated and AMP-dependent protein kinases, myosin light chain kinases, checkpoint 2 kinases (CHK2) and EMK-related protein kinases. The EMK family of STK are involved in the control of cell polarity, microtubule stability and cancer. One member of the EMK family, C-TAK1 has been reported to control entry into mitosis by activating Cdc25C which in turn dephosphorylates Cdc2.

15       CMGC group kinases are "proline-directed" enzymes phosphorylating residues that exist in a proline-rich context. They include the cyclin-dependent kinases (CDKs), mitogen-activated kinases (MAPKs), GSK3s and CLKs. Most CMGC kinases have larger-than-average kinase domains owing to the presence of insertions within subdomains X and XI.

20       The tyrosine kinase group encompass both cytoplasmic (i.e. src) as well as transmembrane receptor tyrosine kinases (i.e. EGF receptor). These kinases play a pivotal role in the signal transduction processes that mediate cell proliferation, differentiation and apoptosis.

25       Group members that define smaller, yet distinct phylogenetic branches of conventional kinases include the elongation factor 2 kinases (EFKs); homologues of the yeast sterile family kinases (STE) which refers to 3 classes of kinases which lie sequentially upstream of the MAPKs; mixed lineage kinases (MLKs); Lim-domain containing kinases (LIMKs); Calcium-calmodulin kinase kinases (CAMKK), dual-specific tyrosine kinases (DYRK), integrin receptor associated kinase (IRAK); testis-specific kinases (TSK); UNC-51 related kinases (UNC); several families that are close  
30       homologues to worm (C26C2.1, YQ09, ZC581.9, YFL033c, C24A1.3), Drosophila (SLOB), or yeast (YDOD\_sp, YGR262\_sc) kinases, and others that are "unique" and don't cluster into any obvious family.

### SUMMARY OF THE INVENTION

Through a search of the EST database for homologies to the conserved catalytic kinase domain of protein kinases, hundreds of mammalian members of known and previously unidentified protein kinase families and groups have been identified as part of the present invention. Multiple alignment and parsimony analysis of the catalytic domain reveals that approximately half of these protein kinases cluster into 10 known groups, with the other half perhaps defining novel groups. Classification in this manner has proven highly accurate not only in predicting motifs present in the remaining non-catalytic portion of each protein, but also in their regulation, substrates, and signaling pathways. The present invention includes the partial or complete sequence of new protein kinases, their classification, predicted or deduced protein structure, and a strategy for elucidating their biologic and therapeutic relevance.

Thus, a first aspect of the invention features an isolated, enriched, or purified nucleic acid molecule encoding a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211.

SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216,  
SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221,  
SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226,  
SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231,  
5 SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236,  
SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241,  
and SEQ ID NO:242.

By "isolated" in reference to nucleic acid is meant a polymer of nucleotides  
conjugated to each other, including DNA and RNA, that is isolated from a natural source  
10 or that is synthesized. The isolated nucleic acid of the present invention is unique in the  
sense that it is not found in a pure or separated state in nature. Use of the term "isolated"  
indicates that a naturally occurring sequence has been removed from its normal cellular  
(i.e., chromosomal) environment. Thus, the sequence may be in a cell-free solution or  
placed in a different cellular environment. The term does not imply that the sequence is  
15 the only nucleotide chain present, but that it is essentially free (about 90 - 95% pure at  
least) of non-nucleotide material naturally associated with it, and thus is distinguished  
from isolated chromosomes.

By the use of the term "enriched" in reference to nucleic acid is meant that the  
specific DNA or RNA sequence constitutes a significantly higher fraction (2 - 5 fold) of  
20 the total DNA or RNA present in the cells or solution of interest than in normal or  
diseased cells or in the cells from which the sequence was taken. This could be caused by  
a person by preferential reduction in the amount of other DNA or RNA present, or by a  
preferential increase in the amount of the specific DNA or RNA sequence, or by a  
combination of the two. However, it should be noted that enriched does not imply that  
25 there are no other DNA or RNA sequences present, just that the relative amount of the  
sequence of interest has been significantly increased. The term "significant" is used to  
indicate that the level of increase is useful to the person making such an increase, and  
generally means an increase relative to other nucleic acids of about at least 2 fold, more  
preferably at least 5 to 10 fold or even more. The term also does not imply that there is no  
30 DNA or RNA from other sources. The other source DNA may, for example, comprise  
DNA from a yeast or bacterial genome, or a cloning vector such as pUC19. This term  
distinguishes from naturally occurring events, such as viral infection, or tumor type

growths, in which the level of one mRNA may be naturally increased relative to other species of mRNA. That is, the term is meant to cover only those situations in which a person has intervened to elevate the proportion of the desired nucleic acid.

It is also advantageous for some purposes that a nucleotide sequence be in purified form. The term "purified" in reference to nucleic acid does not require absolute purity (such as a homogeneous preparation). Instead, it represents an indication that the sequence is relatively more pure than in the natural environment (compared to the natural level this level should be at least 2-5 fold greater, *e.g.*, in terms of mg/mL). Individual clones isolated from a cDNA library may be purified to electrophoretic homogeneity. The claimed DNA molecules obtained from these clones could be obtained directly from total DNA or from total RNA. The cDNA clones are not naturally occurring, but rather are preferably obtained via manipulation of a partially purified naturally occurring substance (messenger RNA). The construction of a cDNA library from mRNA involves the creation of a synthetic substance (cDNA) and pure individual cDNA clones can be isolated from the synthetic library by clonal selection of the cells carrying the cDNA library. Thus, the process which includes the construction of a cDNA library from mRNA and isolation of distinct cDNA clones yields an approximately  $10^6$ -fold purification of the native message. Thus, purification of at least one order of magnitude, preferably two or three orders, and more preferably four or five orders of magnitude is expressly contemplated.

By a "kinase polypeptide" is meant 10 (preferably 20, more preferably 40, most preferably 75) or more contiguous amino acids set forth in an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173,



SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or functional derivatives thereof as described herein. For sequences for which the full-length sequence is not given, the remaining sequences can be determined using methods well-known to those in the art and are intended to be included in the invention. In certain aspects, polypeptides of 100, 200, 300 or more amino acids are preferred. The kinase polypeptide can be encoded by a full-length nucleic acid sequence or any portion of the full-length nucleic acid sequence, so long as a functional activity of the polypeptide is retained. By "functional" domain is meant any region of the polypeptide that may play a regulatory or catalytic role as predicted from amino acid sequence homology to other proteins or by the presence of amino acid sequences that may give rise to specific structural conformations (*i.e.*, coiled-coils). For some purposes, polypeptide domains are preferred, including, but not limited to, N-terminal, catalytic/kinase and C-terminal.

The amino acid sequence will be substantially similar to a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID



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NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID  
NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding  
20 full-length amino acid sequence, or fragments thereof. A sequence that is substantially  
similar to a sequence selected from the group consisting of those set forth in SEQ ID  
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NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ  
ID NO:242 will have at least 75% identity (preferably 90%, more preferably at least 95%  
15 and most preferably 99-100%) to a sequence selected from the group consisting of those  
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ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 or portions of or the entire corresponding full-length amino acid sequences.

By "identity" is meant a property of sequences that measures their similarity or relationship. Identity is measured by dividing the number of identical residues between two sequences (either full-length or a defined domain) by the total number of residues in the known sequence, or the domain of the known sequence, and multiplying the product by 100. Thus, two copies of exactly the same sequence have 100% identity, but sequences that are less highly conserved, and have replacements and substitutions, have a lower degree of identity. "Gaps" are spaces in an alignment that can result from aligning a novel sequence with a known sequence when the novel sequence has additions or deletions of amino acids in comparison with the known sequence. These gaps do not factor into the assessment of % identity using the above calculation.

Those skilled in the art will recognize that several computer programs are also available for determining sequence identity using standard parameters, for example, Blast (Altschul, *et al.* (1997) Nucleic Acids Res. 25:3389-3402), Blast2 (Altschul, *et al.* (1990) J. Mol. Biol. 215:403-410), and Smith-Waterman (Smith, *et al.* (1981) J. Mol. Biol. 147:195-197).

In preferred embodiments, the invention features isolated, enriched, or purified nucleic acid molecules encoding a kinase polypeptide comprising a nucleotide sequence that: (a) encodes a polypeptide having an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ

ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or fragments thereof. A sequence that is substantially similar to a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID

NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID  
NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID  
NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID  
NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID  
5 NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID  
NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID  
NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID  
NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID  
NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID  
10 NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID  
NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID  
NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID  
NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID  
NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 will  
15 have at least 75% identity (preferably 90%, more preferably at least 95% and most  
preferably 99-100%) to the sequence selected from the group consisting of those set forth  
in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID  
NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID  
NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID  
20 NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID  
NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID  
NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID  
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25 NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID  
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30 NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID  
NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID  
NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID



NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID  
NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID  
NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID  
NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID  
5 NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID  
NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID  
NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID  
NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID  
NO:241, and SEQ ID NO:242; (b) is the complement of the nucleotide sequence of (a); (c)  
10 hybridizes under highly stringent conditions to the nucleotide molecule of (a) and encodes  
a naturally occurring kinase polypeptide; (d) encodes a kinase polypeptide having an  
amino acid sequence selected from the group consisting of those set forth in SEQ ID  
NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID  
NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID  
15 NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID  
NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID  
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NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID  
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25 NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID  
NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID  
NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID  
NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID  
NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID  
30 NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID  
NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID  
NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID



NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or fragments thereof.

A sequence that is substantially similar to a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 will have at least 75% identity (preferably 90%, more preferably at least 95% and most preferably 99-100%) to the sequence of SEQ ID

NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it lacks one or more, but not all, of a domain selected from the group consisting of an N-terminal domain, a catalytic domain, a C-terminal domain, a coiled-coil structure region, a proline-rich region, a spacer region, an insert, and a C-terminal tail; (e) is the complement of the nucleotide sequence of (d); (f) encodes a polypeptide having an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID

NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID  
NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID  
NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID  
NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID  
5 NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID  
NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID  
NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID  
NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID  
NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID  
10 NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID  
NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID  
NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID  
NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID  
NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID  
15 NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID  
NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID  
NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID  
NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID  
NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID  
20 NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID  
NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID  
NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or  
fragments thereof. (The domain demarcations of the polypeptides of the invention are  
indicated in Table 2 by reference to the kinase domain.) A sequence that is substantially  
25 similar to a sequence selected from the group consisting of those set forth in SEQ ID  
NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID  
NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID  
NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID  
NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID  
30 NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID  
NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID  
NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID

NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID  
NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID  
NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID  
NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID  
5 NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID  
NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID  
NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID  
NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID  
NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID  
10 NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID  
NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID  
NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID  
NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID  
NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID  
15 NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID  
NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID  
NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ  
ID NO:242 will have at least 75% identity (preferably 90%, more preferably at least 95%  
and most preferably 99-100%) to the sequence selected from the group consisting of those  
20 set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ  
ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ  
ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ  
ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ  
ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ  
25 ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ  
ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ  
ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ  
ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ  
ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ  
30 ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ  
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ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ  
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ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ  
ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ  
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ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ  
ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ  
ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ  
ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ  
ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ  
ID NO:241, and SEQ ID NO:242; (b) is the complement of the nucleotide sequence of (a);  
(c) hybridizes under highly stringent conditions to the nucleotide molecule of (a) and  
encodes a naturally occurring kinase polypeptide; (d) encodes a kinase polypeptide having  
an amino acid sequence selected from the group consisting of those set forth in SEQ ID  
NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID  
NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID  
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NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID  
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NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID  
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NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID



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5 NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID  
NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID  
NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ  
ID NO:242, or the corresponding full-length amino acid sequence, or fragments thereof.

A sequence that is substantially similar to a sequence selected from the group consisting of

10 those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125,  
SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130,  
SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135,  
SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140,  
SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145,  
15 SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150,  
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20 SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175,  
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25 SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200,  
SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205,  
SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210,  
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SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220,  
30 SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225,  
SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230,  
SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235,



SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 will have at least 75% identity (preferably 90%, more preferably at least 95% and most preferably 99-100%) to a domain of a polypeptide selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, where the domain is selected from the group consisting of an N-terminal domain, a catalytic domain, a C-terminal domain, a coiled-coil structure region, a proline-rich region, a spacer region, an insert, and a C-terminal tail; (g) is the complement of the nucleotide sequence of (f); (h) encodes a polypeptide having an amino acid sequence selected from the group consisting

of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or fragments thereof. A sequence that is substantially similar to a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148,

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5 SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173,  
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10 SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198,  
SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203,  
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15 SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223,  
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SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233,  
SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238,  
SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 will have at  
20 least 75% identity (preferably 90%, more preferably at least 95% and most preferably 99-  
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25 NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID  
NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID  
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NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID

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10 NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID  
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NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ  
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25 NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID  
NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID  
NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID  
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NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID  
5 NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID  
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NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID  
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20 SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166,  
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25 SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191,  
SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196,  
SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201,  
SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206,  
SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211,  
30 SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216,  
SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221,  
SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226.



SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 will have at least 75% identity (preferably 90%, more preferably at least 95% and most preferably 99-100%) to the sequence of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it lacks one or more of the domains selected from the group consisting of a N-terminal domain, a catalytic domain, a C-terminal domain, a coiled-coil structure region, a proline-rich region, a spacer region, an insert, and a C-terminal tail; or (i) is the



complement of the nucleotide sequence of (h). The domain demarcations of the polypeptides of the invention are indicated in Table 2 by reference to the kinase domain.

The term "complement" refers to two nucleotides that can form multiple favorable interactions with one another. For example, adenine is complementary to thymine as they can form two hydrogen bonds. Similarly, guanine and cytosine are complementary since they can form three hydrogen bonds. A nucleotide sequence is the complement of another nucleotide sequence if all of the nucleotides of the first sequence are complementary to all of the nucleotides of the second sequence.

The term "domain" refers to a region of a polypeptide that contains a particular function. For instance, N-terminal or C-terminal domains of signal transduction proteins can serve functions including, but not limited to, binding molecules that localize the signal transduction molecule to different regions of the cell or binding other signaling molecules directly responsible for propagating a particular cellular signal. Some domains can be expressed separately from the rest of the protein and function by themselves, while others must remain part of the intact protein to retain function. The latter are termed functional regions of proteins and also relate to domains.

The term "N-terminal domain" refers to the extracatalytic region located between the initiator methionine and the catalytic domain of the protein kinase. The N-terminal domain can be identified following a Smith-Waterman alignment of the protein sequence against the non-redundant protein database to define the N-terminal boundary of the catalytic domain. Depending on its length, the N-terminal domain may or may not play a regulatory role in kinase function. An example of a protein kinase whose N-terminal domain has been shown to play a regulatory role is PAK65, which contains a CRIB motif used for Cdc42 and rac binding (Burbelo, P.D. *et al.* (1995) *J. Biol. Chem.* 270, 29071-29074). The N-terminal domain of a protein kinase of the invention is that portion of the protein kinase to the amino-terminal side of the kinase domain where the kinase domain is identified in Table 2, herein. Further, in some cases, portions of the N-terminal domains of the protein kinases of the invention have not been identified since the entire sequence is not available. However, with the methods described herein, the full-length sequences of the kinases of the invention can be determined and using the approaches described herein the N-terminal domain can be identified.

The term "catalytic domain" or "kinase domain" refers to a region of the protein kinase that is typically 25-300 amino acids long and is responsible for carrying out the phosphate transfer reaction from a high-energy phosphate donor molecule such as ATP or GTP to itself (autophosphorylation) or to other proteins (exogenous phosphorylation).

5 The catalytic domain of protein kinases is made up of 12 subdomains that contain highly conserved amino acid residues, and are responsible for proper polypeptide folding and for catalysis. The catalytic domain can be identified following a Smith-Waterman alignment of the protein sequence against the non-redundant protein database. The catalytic/kinase domains of the protein kinases of the invention are identified in Table 2, herein. Further, 10 in some cases, the complete sequence of the catalytic/kinase domains of the protein kinases of the invention may not have been provided since the entire sequence is not available. However, with the methods described herein, the full-length sequences of the kinases of the invention can be determined, and using the approaches described herein, the catalytic/kinase domain can be identified.

15 The term "catalytic activity", as used herein, defines the rate at which a kinase catalytic domain phosphorylates a substrate. Catalytic activity can be measured, for example, by determining the amount of a substrate converted to a phosphorylated product as a function of time. Catalytic activity can be measured by methods of the invention by 20 holding time constant and determining the concentration of a phosphorylated substrate after a fixed period of time. Phosphorylation of a substrate occurs at the active-site of a protein kinase. The active-site is normally a cavity in which the substrate binds to the protein kinase and is phosphorylated.

The term "substrate" as used herein refers to a molecule phosphorylated by a kinase of the invention. Kinases phosphorylate substrates on serine/threonine or tyrosine 25 amino acids. The molecule may be another protein or a polypeptide.

The term "C-terminal domain" refers to the region located between the catalytic domain and the carboxy-terminal amino acid residue of the protein kinase. The C-terminal domain can be identified by using a Smith-Waterman alignment of the protein sequence against the non-redundant protein database to define the C-terminal boundary of 30 the catalytic domain or of any functional C-terminal extracatalytic domain. Depending on its length and amino acid composition, the C-terminal domain may or may not play a regulatory role in kinase function. An example of a protein kinase whose C-terminal

domain may play a regulatory role is PAK3 which contains a heterotrimeric G<sub>i</sub> subunit-binding site near its C-terminus (Leeuw, T. *et al.* (1998) *Nature*, 391, 191-195). The C-terminal domain of a protein kinase of the invention is that portion of the protein kinase to the carboxy-terminal side of the kinase domain where the kinase domain is identified in Table 2, herein. In some cases, the C-terminal domains of the protein kinases of the invention have not been provided since the entire sequence is not available. However, with the methods described herein, the full-length sequences of the kinases of the invention can be determined, and using the approaches described herein, the C-terminal domain can be identified.

The term "signal transduction pathway" refers to the molecules that propagate an extracellular signal through the cell membrane to become an intracellular signal. This signal can then stimulate a cellular response. The polypeptide molecules involved in signal transduction processes are typically receptor and non-receptor protein tyrosine kinases, receptor and non-receptor protein phosphatases, SRC homology 2 and 3 domains, phosphotyrosine binding proteins (SRC homology 2 (SH2) and phosphotyrosine binding (PTB and PH) domain containing proteins), proline-rich binding proteins (SH3 domain containing proteins), nucleotide exchange factors, and transcription factors.

The term "coiled-coil structure region" as used herein, refers to a polypeptide sequence that has a high probability of adopting a coiled-coil structure as predicted by computer algorithms such as COILS (Lupas, A. (1996) *Meth. Enzymology* 266:513-525). Coiled-coils are formed by two or three amphipathic  $\alpha$ -helices in parallel. Coiled-coils can bind to coiled-coil domains of other polypeptides resulting in homo- or heterodimers (Lupas, A. (1991) *Science* 252:1162-1164). Coiled-coil-dependent oligomerization has been shown to be necessary for protein function including catalytic activity of serine/threonine kinases (Roe, J. *et al.* (1997) *J. Biol. Chem.* 272:5838-5845). Coiled-coil regions in the proteins of the invention can be identified using these methods. They may be present as sub-domains of the N-terminal, kinase, or C-terminal domains of the polypeptides of the invention.

The term "proline-rich region" as used herein, refers to a region of a protein kinase whose proline content over a given amino acid length is higher than the average content of this amino acid found in proteins (*i.e.*, >10%). Proline-rich regions are easily discernable by visual inspection of amino acid sequences and quantitated by standard computer

sequence analysis programs such as the DNASTar program EditSeq. Proline-rich regions have been demonstrated to participate in regulatory protein-protein interactions. Among these interactions, those that are most relevant to this invention involve the "PxxP" proline rich motif found in certain protein kinases (*i.e.*, human PAK1) and the SH3 domain of the adaptor molecule Nck (Galisteo, M.L. *et al.* (1996) J. Biol. Chem. 271:20997-21000).  
5 Other regulatory interactions involving "PxxP" proline-rich motifs include the WW domain (Sudol, M. (1996) Prog. Biophys. Mol. Bio. 65:113-132). Proline rich regions in the proteins of the invention can be identified using these methods. They may be present as sub-domains of the N-terminal, kinase, or C-terminal domains of the polypeptides of  
10 the invention.

The term "spacer region" as used herein, refers to a region of the protein kinase located between predicted functional domains. The spacer region has no detectable homology to any amino acid sequence in the database, and can be identified by using a Smith-Waterman alignment of the protein sequence against the non-redundant protein  
15 database to define the C- and N-terminal boundaries of the flanking functional domains. Spacer regions may or may not play a fundamental role in protein kinase function. Precedence for the regulatory role of spacer regions in kinase function is provided by the role of the src kinase spacer in inter-domain interactions (Xu, W. *et al.* (1997) Nature 385:595-602). Spacer regions in the proteins of the invention can be identified using these  
20 methods. They may be present as sub-domains of the N-terminal, kinase, or C-terminal domains of the polypeptides of the invention.

The term "insert" as used herein refers to a portion of a protein kinase that is absent from a close homolog. Inserts may or may not be the product alternative splicing of exons. Inserts can be identified by using a Smith-Waterman sequence alignment of the  
25 protein sequence against the non-redundant protein database, or by means of a multiple sequence alignment of homologous sequences using the DNASTar program Megalign. Inserts may play a functional role by presenting a new interface for protein-protein interactions, or by interfering with such interactions. Insert regions in the proteins of the invention can be identified using these methods. They may be present as sub-domains of  
30 the N-terminal, kinase, or C-terminal domains of the polypeptides of the invention.

The term "C-terminal tail" as used herein, refers to a C-terminal domain of a protein kinase, that by homology extends or protrudes past the C-terminal amino acid of its closest homolog. C-terminal tails can be identified by using a Smith-Waterman sequence alignment of the protein sequence against the non-redundant protein database, or by means of a multiple sequence alignment of homologous sequences using the DNASTar program Megalign. Depending on its length, a C-terminal tail may or may not play a regulatory role in kinase function. C-terminal tail regions in the proteins of the invention can be identified using these methods. They may be present as sub-domains of the N-terminal, kinase, or C-terminal domains of the polypeptides of the invention.

Various low or high stringency hybridization conditions may be used depending upon the specificity and selectivity desired. These conditions are well-known to those skilled in the art. Under stringent hybridization conditions only highly complementary nucleic acid sequences hybridize. Preferably, such conditions prevent hybridization of nucleic acids having more than 1 or 2 mismatches out of 20 contiguous nucleotides, more preferably, such conditions prevent hybridization of nucleic acids having more than 1 or 2 mismatches out of 50 contiguous nucleotides, most preferably, such conditions prevent hybridization of nucleic acids having more than 1 or 2 mismatches out of 100 contiguous nucleotides. In some instances, the conditions may prevent hybridization of nucleic acids having more than 5 mismatches in the full-length sequence.

By stringent hybridization assay conditions is meant hybridization assay conditions at least as stringent as the following: hybridization in 50% formamide, 5X SSC, 50 mM  $\text{NaH}_2\text{PO}_4$ , pH 6.8, 0.5% SDS, 0.1 mg/mL sonicated salmon sperm DNA, and 5X Denhart solution at 42 °C overnight; washing with 2X SSC, 0.1% SDS at 45 °C; and washing with 0.2X SSC, 0.1% SDS at 45 °C. Under some of the most stringent hybridization assay conditions, the second wash can be done with 0.1X SSC at a temperature up to 70 °C (pg. 421, Berger *et al.* (1987) Guide to Molecular Cloning Techniques, Meth. Enzym. vol. 152, hereby incorporated by reference herein including any figures, tables, or drawings.). However, other applications may require the use of conditions falling between these sets of conditions. Methods of determining the conditions required to achieve desired hybridizations are well-known to those with ordinary skill in the art, and are based on several factors, including but not limited to, the sequences to be hybridized and the samples to be tested.



In other preferred embodiments, the invention features isolated, enriched, or purified nucleic acid molecules encoding kinase polypeptides, further comprising a vector or promoter effective to initiate transcription in a host cell. The invention also features recombinant nucleic acid, preferably in a cell or an organism. The recombinant nucleic acid may contain a sequence selected from the group consisting of those set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, and SEQ ID NO:121, or a functional derivative thereof and a vector or a promoter effective to initiate transcription in a host cell. The recombinant nucleic acid can alternatively contain a transcriptional initiation region functional in a cell, a sequence complementary to an RNA sequence encoding a kinase polypeptide and a transcriptional termination region functional in a cell. Specific

vectors and host cell combinations are discussed herein. The recombinant nucleic acid can also contain the full-length sequence encoding the protein kinase, or a domain, for example.

The term "vector" relates to a single or double-stranded circular nucleic acid molecule that can be transfected into cells and replicated within or independently of a cell genome. A circular double-stranded nucleic acid molecule can be cut and thereby linearized upon treatment with restriction enzymes. An assortment of nucleic acid vectors, restriction enzymes, and the knowledge of the nucleotide sequences cut by restriction enzymes are readily available to those skilled in the art. A nucleic acid molecule encoding a kinase can be inserted into a vector by cutting the vector with restriction enzymes and ligating the two pieces together.

The term "transfecting" defines a number of methods to insert a nucleic acid vector or other nucleic acid molecules into a cellular organism. These methods involve a variety of techniques, such as treating the cells with high concentrations of salt, an electric field, detergent, or DMSO to render the outer membrane or wall of the cells permeable to nucleic acid molecules of interest or use of various viral transduction strategies.

The term "promoter" as used herein, refers to nucleic acid sequence needed for gene sequence expression. Promoter regions vary from organism to organism, but are well known to persons skilled in the art for different organisms. For example, in prokaryotes, the promoter region contains both the promoter (which directs the initiation of RNA transcription) as well as the DNA sequences which, when transcribed into RNA, will signal synthesis initiation. Such regions will normally include those 5'-non-coding sequences involved with initiation of transcription and translation, such as the TATA box, capping sequence, CAAT sequence, and the like.

In preferred embodiments, the isolated nucleic acid comprises, consists essentially of, or consists of a nucleic acid sequence set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35.

SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, and SEQ ID NO:121, or the corresponding full-length sequence, encodes an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID

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NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID  
10 NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ  
ID NO:242, or the corresponding full-length amino acid sequence, a functional derivative  
thereof, or at least 10, 20, 40, 50, 75, 100, 200, 300 or 500 contiguous amino acids of a  
sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID  
NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID  
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NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID  
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NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID  
NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID

NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length sequences or derivatives thereof. The nucleic acid may be isolated from a natural source by cDNA cloning or by subtractive hybridization. The natural source may be mammalian, preferably human, blood, semen, or tissue, and the nucleic acid may be synthesized by the triester method or by using an automated DNA synthesizer.

The term "mammal" refers preferably to such organisms as mice, rats, rabbits, guinea pigs, sheep, and goats, more preferably to cats, dogs, monkeys, and apes, and most preferably to humans.

In yet other preferred embodiments, the nucleic acid is a conserved or unique region, for example those useful for: the design of hybridization probes to facilitate identification and cloning of additional polypeptides, the design of PCR probes to facilitate cloning of additional polypeptides, obtaining antibodies to polypeptide regions, and designing antisense oligonucleotides.

By "conserved nucleic acid regions", are meant regions present on two or more nucleic acids encoding a kinase polypeptide, to which a particular nucleic acid sequence can hybridize under lower stringency conditions. Examples of lower stringency conditions suitable for screening for nucleic acid encoding kinase polypeptides are provided in Berger *et al.* (1987) Guide to Molecular Cloning Techniques, Meth. Enzym. vol. 152, hereby incorporated by reference herein in its entirety, including any drawings, figures, or tables. Preferably, conserved regions differ by no more than 5 out of 20 nucleotides, even more preferably 2 out of 20 nucleotides or most preferably 1 out of 20 nucleotides.

By "unique nucleic acid region" is meant a sequence present in a nucleic acid coding for a kinase polypeptide that is not present in a sequence coding for any other naturally occurring polypeptide. Such regions preferably encode 10 (preferably 25, more preferably 50, most preferably 75) or more contiguous amino acids selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124,



SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129,  
SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134,  
SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139,  
SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144,  
5 SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149,  
SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154,  
SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159,  
SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164,  
SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169,  
10 SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174,  
SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179,  
SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184,  
SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189,  
SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194,  
15 SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199,  
SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204,  
SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209,  
SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214,  
SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219,  
20 SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224,  
SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229,  
SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234,  
SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239,  
SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or functional derivatives thereof.

25 In particular, a unique nucleic acid region is preferably of mammalian origin and preferably human.

A second aspect of the invention features a nucleic acid probe for the detection of nucleic acid encoding a kinase polypeptide in a sample, wherein said polypeptide is selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124,  
30 SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139,

SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144,  
SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149,  
SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154,  
SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159,  
5 SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164,  
SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169,  
SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174,  
SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179,  
SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184,  
10 SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189,  
SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194,  
SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199,  
SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204,  
SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209,  
15 SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214,  
SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219,  
SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224,  
SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229,  
SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234,  
20 SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239,  
SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242. Preferably, the nucleic acid  
probe encodes a kinase polypeptide that is a fragment of the protein encoded by an amino  
acid sequence selected from the group consisting of those set forth in SEQ ID NO:122,  
SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127,  
25 SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132,  
SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137,  
SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142,  
SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147,  
SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152,  
30 SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157,  
SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162,  
SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167,

SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172,  
SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177,  
SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182,  
SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187,  
5 SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199,  
SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197,  
SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202,  
SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207,  
SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212,  
10 SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217,  
SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222,  
SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227,  
SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232,  
SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237,  
15 SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID  
NO:242, or the corresponding full-length amino acid sequences. The nucleic acid probe  
contains a nucleotide base sequence that will hybridize to a sequence selected from the  
group consisting of those set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ  
ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9,  
20 SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ  
ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID  
NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25,  
SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ  
ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID  
25 NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41,  
SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ  
ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID  
NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57,  
SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ  
30 ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID  
NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73,  
SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ

ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, and SEQ ID NO:121, or the corresponding full-length sequence, or a functional derivative thereof.

In preferred embodiments, the nucleic acid probe hybridizes to nucleic acid encoding at least 6, 12, 75, 90, 105, 120, 150, 200, 250, 300 or 350 contiguous amino acids of a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID

NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or functional derivatives thereof.

Methods for using the probes include detecting the presence or amount of kinase RNA in a sample by contacting the sample with a nucleic acid probe under conditions such that hybridization occurs and detecting the presence or amount of the probe bound to kinase RNA. The nucleic acid duplex formed between the probe and a nucleic acid sequence coding for a kinase polypeptide may be used in the identification of the sequence of the nucleic acid detected (Nelson *et al.*, in *Nonisotopic DNA Probe Techniques*, Academic Press, San Diego, Kricka, ed., p. 275, 1992, hereby incorporated by reference herein in its entirety, including any drawings, figures, or tables). Kits for performing such methods may be constructed to include a container means having disposed therein a nucleic acid probe.

In a third aspect, the invention describes a recombinant cell or tissue comprising a nucleic acid molecule encoding a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186,



SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191,  
SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196,  
SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201,  
SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206,  
5 SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211,  
SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216,  
SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221,  
SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226,  
SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231,  
10 SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236,  
SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241,  
and SEQ ID NO:242. In such cells, the nucleic acid may be under the control of the  
genomic regulatory elements, or may be under the control of exogenous regulatory  
elements including an exogenous promoter. By "exogenous" it is meant a promoter that is  
15 not normally coupled *in vivo* transcriptionally to the coding sequence for the kinase  
polypeptides.

The polypeptide is preferably a fragment of the protein encoded by an amino acid  
sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID  
NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID  
20 NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID  
NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID  
NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID  
NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID  
NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID  
25 NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID  
NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID  
NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID  
NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID  
NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID  
30 NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID  
NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID  
NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID

NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID  
NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID  
NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID  
NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID  
5 NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID  
NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID  
NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID  
NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID  
NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID  
10 NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the  
corresponding full-length amino acid sequence. By "fragment," is meant an amino acid  
sequence present in a kinase polypeptide. Preferably, such a sequence comprises at least  
10, 20, 40, 50, 75, 100, 200, or 300 contiguous amino acids a sequence selected from the  
group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124,  
15 SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129,  
SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134,  
SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139,  
SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144,  
SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149,  
20 SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154,  
SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159,  
SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164,  
SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169,  
SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174,  
25 SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179,  
SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184,  
SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189,  
SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194,  
SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199,  
30 SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204,  
SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209,  
SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214,

SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219,  
SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224,  
SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229,  
SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234,  
5 SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239,  
SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or of the corresponding full-  
length amino acid sequence, or a functional derivative thereof.

In a fourth aspect, the invention features an isolated, enriched, or purified kinase  
polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ  
10 ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ  
ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ  
ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ  
ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ  
ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ  
15 ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ  
ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ  
ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ  
ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ  
ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ  
20 ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ  
ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ  
ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ  
ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ  
ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ  
25 ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ  
ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ  
ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ  
ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ  
ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ  
30 ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ  
ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ

ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

By "isolated" in reference to a polypeptide is meant a polymer of amino acids (2 or more amino acids) conjugated to each other, including polypeptides that are isolated from a natural source or that are synthesized. The isolated polypeptides of the present invention are unique in the sense that they are not found in a pure or separated state in nature. Use of the term "isolated" indicates that a naturally occurring sequence has been removed from its normal cellular environment. Thus, the sequence may be in a cell-free solution or placed in a different cellular environment. The term does not imply that the sequence is the only amino acid chain present, but that it is essentially free (about 90 - 95% pure at least) of non-amino acid material naturally associated with it.

By the use of the term "enriched" in reference to a polypeptide is meant that the specific amino acid sequence constitutes a significantly higher fraction (2 - 5 fold) of the total amino acid sequences present in the cells or solution of interest than in normal or diseased cells or in the cells from which the sequence was taken. This could be caused by a person by preferential reduction in the amount of other amino acid sequences present, or by a preferential increase in the amount of the specific amino acid sequence of interest, or by a combination of the two. However, it should be noted that enriched does not imply that there are no other amino acid sequences present, just that the relative amount of the sequence of interest has been significantly increased. The term significant here is used to indicate that the level of increase is useful to the person making such an increase, and generally means an increase relative to other amino acid sequences of about at least 2-fold, more preferably at least 5- to 10-fold or even more. The term also does not imply that there is no amino acid sequence from other sources. The other source of amino acid sequences may, for example, comprise amino acid sequence encoded by a yeast or bacterial genome, or a cloning vector such as pUC19. The term is meant to cover only those situations in which man has intervened to increase the proportion of the desired amino acid sequence.

It is also advantageous for some purposes that an amino acid sequence be in purified form. The term "purified" in reference to a polypeptide does not require absolute purity (such as a homogeneous preparation); instead, it represents an indication that the sequence is relatively purer than in the natural environment. Compared to the natural level

this level should be at least 2-5 fold greater (*e.g.*, in terms of mg/mL). Purification of at least one order of magnitude, preferably two or three orders, and more preferably four or five orders of magnitude is expressly contemplated. The substance is preferably free of contamination at a functionally significant level, for example 90%, 95%, or 99% pure.

5           In preferred embodiments, the kinase polypeptide is a fragment of the protein encoded by an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, 10   SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, 15   SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, 20   SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, 25   SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, 30   SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequences. Preferably, the kinase polypeptide contains at least 10, 20, 40, 50, 75, 100, 200, or 300 contiguous



amino acids a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or a functional derivative thereof.

In preferred embodiments, the kinase polypeptide comprises an amino acid sequence having (a) an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ

ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242; (b) an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ

5 ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ  
ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ  
ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ  
ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ  
ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ  
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ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ  
ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ  
10 ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ  
ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ  
ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ  
ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ  
ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ  
15 ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it lacks one or more, but  
not all, of a domain selected from the group consisting of an N-terminal domain, a  
catalytic domain, a C-terminal domain, a coiled-coil structure region, a proline-rich region,  
a spacer region, an insert, and a C-terminal tail; (c) an amino acid sequence of a domain of  
a polypeptide selected from the group consisting of those set forth in SEQ ID NO:122,  
20 SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127,  
SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132,  
SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137,  
SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142,  
SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147,  
25 SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152,  
SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157,  
SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162,  
SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167,  
SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172,  
30 SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177,  
SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182,  
SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187,

SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199,  
SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197,  
SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202,  
SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207,  
5 SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212,  
SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217,  
SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222,  
SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227,  
SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232,  
10 SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237,  
SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID  
NO:242 where the domain is selected from the group consisting of an N-terminal domain,  
a catalytic domain, a C-terminal domain, a coiled-coil structure region, a proline-rich  
region, a spacer region, an insert, and a C-terminal tail; or (d) an amino acid sequence  
15 selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123,  
SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128,  
SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133,  
SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138,  
SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143,  
20 SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148,  
SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153,  
SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158,  
SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163,  
SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168,  
25 SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173,  
SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178,  
SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183,  
SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188,  
SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193,  
30 SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198,  
SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203,  
SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208,

SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213,  
SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218,  
SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223,  
SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228,  
5 SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233,  
SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238,  
SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it  
lacks one or more, but not all, of the domains selected from the group consisting of a C-  
terminal domain, a catalytic domain, an N-terminal domain, a spacer region, a proline-rich  
10 region, a coiled-coil structure region, an insert, and a C-terminal tail. (The domain  
demarcations of the polypeptides of the invention are indicated in Table 2 by reference to  
the kinase domain.)

The polypeptide can be isolated from a natural source by methods well-known in  
the art. The natural source may be mammalian, preferably human, blood, semen, or tissue,  
15 and the polypeptide may be synthesized using an automated polypeptide synthesizer. The  
isolated, enriched, or purified kinase polypeptide is preferably selected from the group  
consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ  
ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ  
ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ  
20 ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ  
ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ  
ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ  
ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ  
ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ  
25 ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ  
ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ  
ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ  
ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ  
ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ  
30 ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ  
ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ  
ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ



ID NO:200, SEQ ID NO 201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO 206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO 218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242A.

10 In some embodiments the invention includes a recombinant kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229,

SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242. By "recombinant kinase polypeptide" is meant a polypeptide produced by recombinant DNA techniques such that it is distinct from a naturally occurring polypeptide either in its location (*e.g.*, present in a different cell or tissue than found in nature), purity or structure. Generally, such a recombinant polypeptide will be present in a cell in an amount different from that normally observed in nature.

In a fifth aspect, the invention features an antibody (*e.g.*, a monoclonal or polyclonal antibody) having specific binding affinity to a kinase polypeptide or a kinase polypeptide domain or fragment where the polypeptide is selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ

ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242. In preferred embodiments, the antibody binds specifically to domains of kinase polypeptides, that are defined *supra*.

By "specific binding affinity" is meant that the antibody binds to the target kinase polypeptide with greater affinity than it binds to other polypeptides under specified conditions. Antibodies or antibody fragments are polypeptides that contain regions that can bind other polypeptides. The term "specific binding affinity" describes an antibody that binds to a kinase polypeptide with greater affinity than it binds to other polypeptides under specified conditions.

The term "polyclonal" refers to antibodies that are heterogenous populations of antibody molecules derived from the sera of animals immunized with an antigen or an antigenic functional derivative thereof. For the production of polyclonal antibodies, various host animals may be immunized by injection with the antigen. Various adjuvants may be used to increase the immunological response, depending on the host species.

"Monoclonal antibodies" are substantially homogenous populations of antibodies to a particular antigen. They may be obtained by any technique which provides for the production of antibody molecules by continuous cell lines in culture. Monoclonal antibodies may be obtained by methods known to those skilled in the art (Kohler *et al.*, Nature 256:495-497, 1975, and U.S. Patent No. 4,376,110, both of which are hereby incorporated by reference herein in their entirety including any figures, tables, or drawings).

The term "antibody fragment" refers to a portion of an antibody, often the hyper variable region and portions of the surrounding heavy and light chains, that displays specific binding affinity for a particular molecule. A hyper variable region is a portion of an antibody that physically binds to the polypeptide target.

Antibodies or antibody fragments having specific binding affinity to a kinase polypeptide or domains of a kinase polypeptide of the invention may be used in methods for detecting the presence and/or amount of kinase polypeptide in a sample by probing the sample with the antibody under conditions suitable for kinase-antibody immunocomplex formation and detecting the presence and/or amount of the antibody conjugated to the

kinase polypeptide. Diagnostic kits for performing such methods may be constructed to include antibodies or antibody fragments specific for the kinase as well as a conjugate of a binding partner of the antibodies or the antibodies themselves.

An antibody or antibody fragment with specific binding affinity to a kinase polypeptide of the invention can be isolated, enriched, or purified from a prokaryotic or eukaryotic organism. Routine methods known to those skilled in the art enable production of antibodies or antibody fragments, in both prokaryotic and eukaryotic organisms. Purification, enrichment, and isolation of antibodies, which are polypeptide molecules, are described above.

Antibodies having specific binding affinity to a kinase polypeptide of the invention may be used in methods for detecting the presence and/or amount of kinase polypeptide in a sample by contacting the sample with the antibody under conditions such that an immunocomplex forms and detecting the presence and/or amount of the antibody conjugated to the kinase polypeptide. Diagnostic kits for performing such methods may be constructed to include a first container containing the antibody and a second container having a conjugate of a binding partner of the antibody and a label, such as, for example, a radioisotope. The diagnostic kit may also include notification of an FDA approved use and instructions therefor.

In a sixth aspect, the invention features a hybridoma which produces an antibody having specific binding affinity to a kinase polypeptide or a kinase polypeptide domain, where the polypeptide is selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID

NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242; and where the domains are defined as above. By "hybridoma" is meant an immortalized cell line that is capable of secreting an antibody, for example an antibody to a kinase of the invention. In preferred embodiments, the antibody to the kinase comprises a sequence of amino acids that is able to specifically bind a kinase polypeptide of the invention.

In a seventh aspect, the invention features a kinase polypeptide binding agent able to bind to a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187,



SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199,  
SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197,  
SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202,  
SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207,  
5 SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212,  
SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217,  
SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222,  
SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227,  
SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232,  
10 SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237,  
SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID

NO:242. The binding agent is preferably a purified antibody that recognizes an epitope  
present on a kinase polypeptide of the invention. Other binding agents include molecules  
that bind to kinase polypeptides and analogous molecules that bind to a kinase  
15 polypeptide. Such binding agents may be identified by using assays that measure kinase  
binding partner activity, such as those that measure PDGFR activity.

The invention also features a method for screening for human cells containing a  
kinase polypeptide of the invention or an equivalent sequence. The method involves  
identifying the novel polypeptide in human cells using techniques that are routine and  
20 standard in the art, such as those described herein for identifying the kinases of the  
invention (*e.g.*, cloning, Southern or Northern blot analysis, in situ hybridization, PCR  
amplification, etc.).

In an eighth aspect, the invention features methods for identifying a substance that  
modulates kinase activity comprising the steps of: (a) contacting a kinase polypeptide  
25 selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124,  
SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129,  
SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134,  
SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139,  
SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144,  
30 SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149,  
SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154,  
SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159,

SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164,  
SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169,  
SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174,  
SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179,  
5 SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184,  
SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189,  
SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194,  
SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199,  
SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204,  
10 SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209,  
SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214,  
SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219,  
SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224,  
SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229,  
15 SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234,  
SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239,  
SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 with a test substance; (b)  
measuring the activity of said polypeptide; and (c) determining whether said substance  
modulates the activity of said polypeptide.

20 The term "modulates" refers to the ability of a compound to alter the function of a  
kinase of the invention. A modulator preferably activates or inhibits the activity of a  
kinase of the invention.

The term "activates" refers to increasing the cellular activity of the kinase. The  
term inhibit refers to decreasing the cellular activity of the kinase. Kinase activity is  
25 preferably the interaction with a natural binding partner.

The term "modulates" also refers to altering the function of kinases of the  
invention by increasing or decreasing the probability that a complex forms between the  
kinase and a natural binding partner. A modulator preferably increases the probability that  
such a complex forms between the kinase and the natural binding partner, more preferably  
30 increases or decreases the probability that a complex forms between the kinase and the  
natural binding partner depending on the concentration of the compound exposed to the

kinase, and most preferably decreases the probability that a complex forms between the kinase and the natural binding partner.

The term "complex" refers to an assembly of at least two molecules bound to one another. Signal transduction complexes often contain at least two protein molecules bound to one another. For instance, a protein tyrosine receptor protein kinase, GRB2, SOS, RAF, and RAS assemble to form a signal transduction complex in response to a mitogenic ligand.

The term "natural binding partner" refers to polypeptides, lipids, small molecules, or nucleic acids that bind to kinases in cells. A change in the interaction between a kinase and a natural binding partner can manifest itself as an increased or decreased probability that the interaction forms, or an increased or decreased concentration of kinase/natural binding partner complex.

The term "contacting" as used herein refers to mixing a solution comprising the test compound with a liquid medium bathing the cells of the methods. The solution comprising the compound may also comprise another component, such as dimethyl sulfoxide (DMSO), which facilitates the uptake of the test compound or compounds into the cells of the methods. The solution comprising the test compound may be added to the medium bathing the cells by utilizing a delivery apparatus, such as a pipet-based device or syringe-based device.

In a ninth aspect, the invention features methods for identifying a substance that modulates kinase activity in a cell comprising the steps of: (a) expressing a kinase polypeptide in a cell, wherein said polypeptide is selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO 146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO 151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO 156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO 161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO 166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO.171,

SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176,  
SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181,  
SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186,  
SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191,  
5 SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196,  
SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201,  
SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206,  
SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211,  
SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216,  
10 SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221,  
SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226,  
SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231,  
SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236,  
SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241,  
15 and SEQ ID NO:242; (b) adding a test substance to said cell; and (c) monitoring a change  
in cell phenotype or the interaction between said polypeptide and a natural binding  
partner.

The term "expressing" as used herein refers to the production of kinases of the  
invention from a nucleic acid vector containing kinase genes within a cell. The nucleic  
20 acid vector is transfected into cells using well known techniques in the art as described  
herein.

In a tenth aspect, the invention provides methods for treating a disease or abnormal  
condition by administering to a patient in need of such treatment a substance that  
modulates the activity of a polypeptide selected from the group consisting of SEQ ID  
25 NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID  
NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID  
NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID  
NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID  
NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID  
30 NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID  
NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID  
NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID

NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242. Preferably, the disease is selected from the group consisting of immune-related diseases and disorders, cardiovascular disease, neurodegenerative disorders, and cancer. Also included are metabolic disorders, such as diabetes mellitus, and reproductive disorders, such as infertility.

Preferably, the disease or disorder is selected from the group consisting of rheumatoid arthritis, arteriosclerosis, autoimmune disorders, and organ transplantation. Preferably the disease or disorder is selected from the group consisting of immune-related diseases and disorders, myocardial infarction, cardiomyopathies, stroke, renal failure, and oxidative stress-related neurodegenerative disorders. Most preferably, the immune-related diseases and disorders are selected from the group consisting of rheumatoid arthritis, chronic inflammatory bowel disease, chronic inflammatory pelvic disease, multiple sclerosis, asthma, osteoarthritis, psoriasis, arteriosclerosis, rhinitis, autoimmunity, and organ transplantation.

Substances useful for treatment of disorders or diseases preferably show positive results in one or more in vitro assays for an activity corresponding to treatment of the disease or disorder in question. Substances that modulate the activity of the polypeptides



preferably include, but are not limited to, antisense oligonucleotides and inhibitors of protein kinases.

The term "preventing" refers to decreasing the probability that an organism contracts or develops an abnormal condition.

5 The term "treating" refers to having a therapeutic effect and at least partially alleviating or abrogating an abnormal condition in the organism.

The term "therapeutic effect" refers to the inhibition or activation factors causing or contributing to the abnormal condition. A therapeutic effect relieves to some extent one or more of the symptoms of the abnormal condition. In reference to the treatment of  
10 abnormal conditions, a therapeutic effect can refer to one or more of the following: (a) an increase in the proliferation, growth, and/or differentiation of cells; (b) inhibition (*i.e.*, slowing or stopping) of cell death; (c) inhibition of degeneration; (d) relieving to some extent one or more of the symptoms associated with the abnormal condition; and (e) enhancing the function of the affected population of cells. Compounds demonstrating  
15 efficacy against abnormal conditions can be identified as described herein.

The term "abnormal condition" refers to a function in the cells or tissues of an organism that deviates from their normal functions in that organism. An abnormal condition can relate to cell proliferation, cell differentiation or cell survival. An abnormal condition may also include irregularities in cell cycle progression, *i.e.*, irregularities in  
20 normal cell cycle progression through mitosis and meiosis.

Abnormal cell proliferative conditions include cancers such as fibrotic and mesangial disorders, abnormal angiogenesis and vasculogenesis, wound healing, psoriasis, diabetes mellitus, and inflammation.

Abnormal differentiation conditions include, but are not limited to  
25 neurodegenerative disorders, slow wound healing rates, and slow tissue grafting healing rates.

Abnormal cell survival conditions relate to conditions in which programmed cell death (apoptosis) pathways are activated or abrogated. A number of protein kinases are associated with the apoptosis pathways. Aberrations in the function of any one of the  
30 protein kinases could lead to cell immortality or premature cell death.

The term "aberration", in conjunction with the function of a kinase in a signal transduction process, refers to a kinase that is over- or under-expressed in an organism, mutated such that its catalytic activity is lower or higher than wild-type protein kinase activity, mutated such that it can no longer interact with a natural binding partner, is no longer modified by another protein kinase or protein phosphatase, or no longer interacts with a natural binding partner.

The term "administering" relates to a method of incorporating a compound into cells or tissues of an organism. The abnormal condition can be prevented or treated when the cells or tissues of the organism exist within the organism or outside of the organism. Cells existing outside the organism can be maintained or grown in cell culture dishes. For cells harbored within the organism, many techniques exist in the art to administer compounds, including (but not limited to) oral, parenteral, dermal, injection, and aerosol applications. For cells outside of the organism, multiple techniques exist in the art to administer the compounds, including (but not limited to) cell microinjection techniques, transformation techniques, and carrier techniques.

The abnormal condition can also be prevented or treated by administering a compound to a group of cells having an aberration in a signal transduction pathway to an organism. The effect of administering a compound on organism function can then be monitored. The organism is preferably a mouse, rat, rabbit, guinea pig, or goat, more preferably a monkey or ape, and most preferably a human.

In an eleventh aspect, the invention features methods for detection the expression of a polypeptide in a sample as a diagnostic tool for diseases or disorders, wherein the method comprises the steps of: (a) contacting the sample with a nucleic acid probe which hybridizes under hybridization assay conditions to a nucleic acid target region of a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ

ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, said probe comprising the nucleic acid sequence encoding the polypeptide, fragments thereof, and the complements of the sequences and fragments; and (b) detecting the presence or amount of the probe:target region hybrid as an indication of the disease.

In preferred embodiments of the invention, the disease or disorder is selected from the group consisting of rheumatoid arthritis, arteriosclerosis, autoimmune disorders, organ transplantation, myocardial infarction, cardiomyopathies, stroke, renal failure, oxidative stress-related neurodegenerative disorders, metabolic disorder including diabetes, reproductive disorders including infertility, and cancer.

The kinase "target region" is a nucleotide base sequence selected from the group consisting of those set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID

NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36,  
SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ  
ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID  
NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52,  
5 SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ  
ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID  
NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68,  
SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ  
ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID  
10 NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84,  
SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ  
ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID  
NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID  
NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID  
15 NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID  
NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID  
NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID  
NO:120, and SEQ ID NO:121, or the corresponding full-length sequences, a functional  
derivative thereof, or a fragment thereof to which the nucleic acid probe will specifically  
20 hybridize. Specific hybridization indicates that in the presence of other nucleic acids the  
probe only hybridizes detectably with the kinase of the invention's target region. Putative  
target regions can be identified by methods well known in the art consisting of alignment  
and comparison of the most closely related sequences in the database.

In preferred embodiments the nucleic acid probe hybridizes to a kinase target  
25 region encoding at least 6, 12, 75, 90, 105, 120, 150, 200, 250, 300 or 350 contiguous  
amino acids of the sequence set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID  
NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID  
NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID  
NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID  
30 NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID  
NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID  
NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID

NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID  
NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID  
NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID  
NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID  
5 NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID  
NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID  
NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID  
NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID  
NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID  
10 NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID  
NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID  
NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID  
NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID  
NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID  
15 NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID  
NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID  
NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID  
NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding

full-length amino acid sequence, or a functional derivative thereof. Hybridization  
20 conditions should be such that hybridization occurs only with the kinase genes in the  
presence of other nucleic acid molecules. Under stringent hybridization conditions only  
highly complementary nucleic acid sequences hybridize. Preferably, such conditions  
prevent hybridization of nucleic acids having more than 1 or 2 mismatches out of 20  
contiguous nucleotides. Such conditions are defined *supra*.

25 Hybridization conditions should be such that hybridization occurs only with the  
genes in the presence of other nucleic acid molecules. Under stringent hybridization  
conditions only highly complementary nucleic acid sequences hybridize. Preferably, such  
conditions prevent hybridization of nucleic acids having 1 or 2 mismatches out of 20  
contiguous nucleotides. Such conditions are defined *supra*.

30 The diseases for which detection of kinase genes in a sample could be diagnostic  
include diseases in which kinase nucleic acid (DNA and/or RNA) is amplified in  
comparison to normal cells. By "amplification" is meant increased numbers of kinase



DNA or RNA in a cell compared with normal cells. In normal cells, kinases are typically found as single copy genes. In selected diseases, the chromosomal location of the kinase genes may be amplified, resulting in multiple copies of the gene, or amplification. Gene amplification can lead to amplification of kinase RNA, or kinase RNA can be amplified in the absence of kinase DNA amplification.

"Amplification" as it refers to RNA can be the detectable presence of kinase RNA in cells, since in some normal cells there is no basal expression of kinase RNA. In other normal cells, a basal level of expression of kinase exists, therefore in these cases amplification is the detection of at least 1-2-fold, and preferably more, kinase RNA, compared to the basal level.

The diseases that could be diagnosed by detection of kinase nucleic acid in a sample preferably include cancers. The test samples suitable for nucleic acid probing methods of the present invention include, for example, cells or nucleic acid extracts of cells, or biological fluids. The samples used in the above-described methods will vary based on the assay format, the detection method and the nature of the tissues, cells or extracts to be assayed. Methods for preparing nucleic acid extracts of cells are well known in the art and can be readily adapted in order to obtain a sample that is compatible with the method utilized.

Another aspect of the invention involves a method of agonizing (stimulating) or antagonizing a target of the invention and a natural binding partner associated activity in a mammal comprising administering to said mammal an agonist or antagonist to one of the above disclosed polypeptides in an amount sufficient to effect said agonism or antagonism. A method of treating diseases in a mammal with an agonist or antagonist of the protein of the present invention activity comprising administering the agonist or antagonist to a mammal in an amount sufficient to agonize or antagonize associated functions is also encompassed in the present application.

In an effort to discover novel treatments for diseases, biomedical researchers and chemists have designed, synthesized, and tested molecules that inhibit the function of protein polypeptides. Some small organic molecules form a class of compounds that modulate the function of protein polypeptides. Examples of molecules that have been reported to inhibit the function of protein kinases include, but are not limited to, bis monocyclic, bicyclic or heterocyclic aryl compounds (PCT WO 92/20642, published

November 26, 1992 by Maguire *et al.*), vinylene-azaindole derivatives (PCT WO 94 14808, published July 7, 1994 by Ballinari *et al.*), 1-cyclopropyl-4-pyridyl-quinolones (U.S. Patent No. 5,330,992), styryl compounds (U.S. Patent No. 5,217,999), styryl-substituted pyridyl compounds (U.S. Patent No. 5,302,606), certain quinazoline derivatives (EP Application No. 0 566 266 A1), seleoindoles and selenides (PCT WO 94/03427, published February 17, 1994 by Denny *et al.*), tricyclic polyhydroxylic compounds (PCT WO 92/21660, published December 10, 1992 by Dow), and benzylphosphonic acid compounds (PCT WO 91/15495, published October 17, 1991 by Dow *et al.*), all of which are incorporated by reference herein, including any drawings.

Compounds that can traverse cell membranes and are resistant to acid hydrolysis are potentially advantageous as therapeutics as they can become highly bioavailable after being administered orally to patients. However, many of these protein inhibitors only weakly inhibit function. In addition, many inhibit a variety of protein kinases and will therefore cause multiple side-effects as therapeutics for diseases.

Some indolinone compounds, however, form classes of acid resistant and membrane permeable organic molecules. WO 96/22976 (published August 1, 1996 by Ballinari *et al.*) describes hydrosoluble indolinone compounds that harbor tetralin, naphthalene, quinoline, and indole substituents fused to the oxindole ring. These bicyclic substituents are in turn substituted with polar groups including hydroxylated alkyl, phosphate, and ether substituents. U.S. Patent Application Serial Nos. 08/702,232, filed August 23, 1996, entitled "Indolinone Combinatorial Libraries and Related Products and Methods for the Treatment of Disease" by Tang *et al.* (Lyon & Lyon Docket No. 221/187) and 08/485,323, filed June 7, 1995, entitled "Benzylidene-Z-Indoline Compounds for the Treatment of Disease" by Tang *et al.* (Lyon & Lyon Docket No. 223/298) and International Patent Publication WO 96/22976, published August 1, 1996 by Ballinari *et al.*, all of which are incorporated herein by reference in their entirety, including any drawings, describe indolinone chemical libraries of indolinone compounds harboring other bicyclic moieties as well as monocyclic moieties fused to the oxindole ring. Applications 08/702,232, filed August 23, 1996, entitled "Indolinone Combinatorial Libraries and Related Products and Methods for the Treatment of Disease" by Tang *et al.* (Lyon & Lyon Docket No. 221/187), 08/485,323, filed June 7, 1995, entitled "Benzylidene-Z-Indoline Compounds for the Treatment of Disease" by Tang *et al.* (Lyon

& Lyon Docket No. 223/298), and WO 96/22976, published August 1, 1996 by Ballinari *et al.* teach methods of indolinone synthesis, methods of testing the biological activity of indolinone compounds in cells, and inhibition patterns of indolinone derivatives, both of which are incorporated by reference herein, including any drawings.

5           Other examples of substances capable of modulating kinase activity include, but are not limited to, tyrphostins, quinazolines, quinoxolines, and quinolines. The quinazolines, tyrphostins, quinolines, and quinoxolines referred to above include well known compounds such as those described in the literature. For example, representative publications describing quinazolines include Barker *et al.*, EPO Publication No. 0 520 722  
10   A1; Jones *et al.*, U.S. Patent No. 4,447,608; Kabbe *et al.*, U.S. Patent No. 4,757,072; Kaul and Vougioukas, U.S. Patent No. 5, 316,553; Kreighbaum and Comer, U.S. Patent No. 4,343,940; Pegg and Wardleworth, EPO Publication No. 0 562 734 A1; Barker *et al.*, Proc. of Am. Assoc. for Cancer Research 32:327 (1991); Bertino, J.R., Cancer Research 3:293-304 (1979); Bertino, J.R., Cancer Research 9(2 part 1):293-304 (1979); Curtin *et al.*, Br. J. Cancer 53:361-368 (1986); Fernandes *et al.*, Cancer Research 43:1117-1123 (1983); Ferris  
15   *et al.* J. Org. Chem. 44(2):173-178; Fry *et al.*, Science 265:1093-1095 (1994); Jackman *et al.*, Cancer Research 51:5579-5586 (1981); Jones *et al.* J. Med. Chem. 29(6):1114-1118; Lee and Skibo, Biochemistry 26(23):7355-7362 (1987); Lemus *et al.*, J. Org. Chem. 54:3511-3518 (1989); Ley and Seng, Synthesis 1975:415-522 (1975); Maxwell *et al.*,  
20   Magnetic Resonance in Medicine 17:189-196 (1991); Mini *et al.*, Cancer Research 45:325-330 (1985); Phillips and Castle, J. Heterocyclic Chem. 17(19):1489-1596 (1980); Reece *et al.*, Cancer Research 47(11):2996-2999 (1977); Sculier *et al.*, Cancer Immunol. and Immunother. 23:A65 (1986); Sikora *et al.*, Cancer Letters 23:289-295 (1984); and Sikora *et al.*, Analytical Biochem. 172:344-355 (1988), all of which are incorporated  
25   herein by reference in their entirety, including any drawings.

Quinoxaline is described in Kaul and Vougioukas, U.S. Patent No. 5,316,553, incorporated herein by reference in its entirety, including any drawings.

Quinolines are described in Dolle *et al.*, J. Med. Chem. 37:2627-2629 (1994); MaGuire, J. Med. Chem. 37:2129-2131 (1994); Burke *et al.*, J. Med. Chem. 36:425-432  
30   (1993); and Burke *et al.* BioOrganic Med. Chem. Letters 2:1771-1774 (1992), all of which are incorporated by reference in their entirety, including any drawings.

Tyrphostins are described in Allen et al., Clin. Exp. Immunol. 91:141-156 (1993); Anafi et al., Blood 82:12:3524-3529 (1993); Baker et al., J. Cell Sci. 102:543-555 (1992); Bilder et al., Amer. Physiol. Soc. pp. 6363-6143:C721-C730 (1991); Brunton et al., Proceedings of Amer. Assoc. Cancer Rsch. 33:558 (1992); Bryckaert et al., Experimental  
5 Cell Research 199:255-261 (1992); Dong et al., J. Leukocyte Biology 53:53-60 (1993); Dong et al., J. Immunol. 151(5):2717-2724 (1993); Gazit et al., J. Med. Chem. 32:2344-2352 (1989); Gazit et al., "J. Med. Chem. 36:3556-3564 (1993); Kaur et al., Anti-Cancer Drugs 5:213-222 (1994); Kaur et al., King et al., Biochem. J. 275:413-418 (1991); Kuo et al., Cancer Letters 74:197-202 (1993); Levitzki, A., The FASEB J. 6:3275-3282 (1992);  
10 Lyall et al., J. Biol. Chem. 264:14503-14509 (1989); Peterson et al., The Prostate 22:335-345 (1993); Pillemer et al., Int. J. Cancer 50:80-85 (1992); Posner et al., Molecular Pharmacology 45:673-683 (1993); Rendu et al., Biol. Pharmacology 44(5):881-888 (1992); Sauro and Thomas, Life Sciences 53:371-376 (1993); Sauro and Thomas, J. Pharm. and Experimental Therapeutics 267(3):119-1125 (1993); Wolbring et al., J. Biol. Chem. 269(36):22470-22472 (1994); and Yoneda et al., Cancer Research 51:4430-4435 (1991); all of which are incorporated herein by reference in their entirety, including any drawings.

Other compounds that could be used as modulators include oxindolinones such as those described in U.S. patent application Serial No. 08/702,232 filed August 23, 1996,  
20 incorporated herein by reference in its entirety, including any drawings.

#### Methods of Treating a Disease (Enablement - i.e., Dosing)

Methods of determining the dosages of compounds to be administered to a patient and modes of administering compounds to an organism are disclosed in U.S. Application Serial No. 08/702,282, filed August 23, 1996 and International patent publication number  
25 WO 96/22976, published August 1 1996, both of which are incorporated herein by reference in their entirety, including any drawings, figures or tables. Those skilled in the art will appreciate that such descriptions are applicable to the present invention and can be easily adapted to it.

The proper dosage depends on various factors such as the type of disease being  
30 treated, the particular composition being used and the size and physiological condition of the patient. Therapeutically effective doses for the compounds described herein can be estimated initially from cell culture and animal models. For example, a dose can be

formulated in animal models to achieve a circulating concentration range that initially takes into account the  $IC_{50}$  as determined in cell culture assays. The animal model data can be used to more accurately determine useful doses in humans.

Plasma half-life and biodistribution of the drug and metabolites in the plasma, tumors and major organs can also be determined to facilitate the selection of drugs most appropriate to inhibit a disorder. Such measurements can be carried out. For example, HPLC analysis can be performed on the plasma of animals treated with the drug and the location of radiolabeled compounds can be determined using detection methods such as X-ray, CAT scan and MRI. Compounds that show potent inhibitory activity in the screening assays, but have poor pharmacokinetic characteristics, can be optimized by altering the chemical structure and retesting. In this regard, compounds displaying good pharmacokinetic characteristics can be used as a model.

Toxicity studies can also be carried out by measuring the blood cell composition. For example, toxicity studies can be carried out in a suitable animal model as follows:

1) the compound is administered to mice (an untreated control mouse should also be used); 2) blood samples are periodically obtained via the tail vein from one mouse in each treatment group; and 3) the samples are analyzed for red and white blood cell counts, blood cell composition and the percent of lymphocytes versus polymorphonuclear cells. A comparison of results for each dosing regime with the controls indicates if toxicity is present.

At the termination of each toxicity study, further studies can be carried out by sacrificing the animals (preferably, in accordance with the American Veterinary Medical Association guidelines Report of the American Veterinary Medical Assoc. Panel on Euthanasia, Journal of American Veterinary Medical Assoc., 202:229-249, 1993).

Representative animals from each treatment group can then be examined by gross necropsy for immediate evidence of metastasis, unusual illness or toxicity. Gross abnormalities in tissue are noted and tissues are examined histologically. Compounds causing a reduction in body weight or blood components are less preferred, as are compounds having an adverse effect on major organs. In general, the greater the adverse effect the less preferred the compound.



For the treatment of cancers the expected daily dose of a hydrophobic pharmaceutical agent is between 1 to 500 mg/day, preferably 1 to 250 mg/day, and most preferably 1 to 50 mg/day. Drugs can be delivered less frequently provided plasma levels of the active moiety are sufficient to maintain therapeutic effectiveness.

5 Plasma levels should reflect the potency of the drug. Generally, the more potent the compound the lower the plasma levels necessary to achieve efficacy.

In a final aspect, the invention features a method for detection of a kinase polypeptide in a sample as a diagnostic tool for a disease or disorder, wherein the method comprises: (a) comparing a nucleic acid target region encoding the kinase polypeptide in  
10 a sample, where the kinase polypeptide is selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID  
15 NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID  
20 NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID

NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or one or more fragments thereof, with a control nucleic acid target region encoding the kinase polypeptide, or one or more fragments thereof; and (b) detecting  
5 differences in sequence or amount between the target region and the control target region, as an indication of the disease or disorder. Preferably, the disease or disorder is selected from the group consisting of immune-related diseases and disorders, organ transplantation, myocardial infarction, cardiovascular disease, stroke, renal failure, oxidative stress-related neurodegenerative disorders, and cancer. Immune-related diseases and disorders include,  
10 but are not limited to, those discussed previously.

The term "comparing" as used herein refers to identifying discrepancies between the nucleic acid target region isolated from a sample, and the control nucleic acid target region. The discrepancies can be in the nucleotide sequences, *e.g.* insertions, deletions, or point mutations, or in the amount of a given nucleotide sequence. Methods to determine  
15 these discrepancies in sequences are well-known to one of ordinary skill in the art. The "control" nucleic acid target region refers to the sequence or amount of the sequence found in normal cells, *e.g.* cells that are not diseased as discussed previously.

The term also includes anti-sense molecules drawn thereto.

The invention has been described broadly and generically herein. Each of the  
20 narrower species and subgeneric groupings falling within the generic disclosure also form part of the invention. This includes the generic description of the invention with a proviso or negative limitation removing any subject matter from the genus, regardless of whether or not the excised material is specifically recited herein. For example, in some instances the nucleotide sequence of particular kinase polypeptides may not be part of a preferred  
25 embodiment.

The summary of the invention described above is not limiting and other features and advantages of the invention will be apparent from the following detailed description of the invention, and from the claims.

BRIEF DESCRIPTION OF THE FIGURES

Figures 1A to 1BB shows the amino acid sequences of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

Figures 2A to 2MMMM shows the nucleic acid sequences of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID

NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34,  
SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ  
ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID  
NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50,  
5 SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ  
ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID  
NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66,  
SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ  
ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID  
10 NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82,  
SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ  
ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID  
NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98,  
SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103,  
15 SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108,  
SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113,  
SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118,  
SEQ ID NO:119, SEQ ID NO:120, and SEQ ID NO:121.

## 20 DETAILED DESCRIPTION OF THE INVENTION

The present invention relates in part to kinase polypeptides, nucleic acids encoding  
such polypeptides, cells containing such nucleic acids, antibodies to such polypeptides,  
assays utilizing such polypeptides, and methods relating to all of the foregoing. The  
present invention is based upon the isolation and characterization of new kinase  
25 polypeptides. The polypeptides and nucleic acids may be produced using well-known and  
standard synthesis techniques when given the sequences presented herein.

### I. The Nucleic Acids of the Invention

Included within the scope of this invention are the functional equivalents of the  
30 herein-described isolated nucleic acid molecules. The degeneracy of the genetic code  
permits substitution of certain codons by other codons that specify the same amino acid  
and hence would give rise to the same protein. The nucleic acid sequence can vary

substantially since, with the exception of methionine and tryptophan, the known amino acids can be coded for by more than one codon. Thus, portions or all of the kinase genes of the invention could be synthesized to give a nucleic acid sequence significantly different from one selected from the group consisting of those set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, and SEQ ID NO:121. The encoded amino acid sequence thereof would, however, be preserved.

In addition, the nucleic acid sequence may comprise a nucleotide sequence which results from the addition, deletion or substitution of at least one nucleotide to the 5'-end and/or the 3'-end of the nucleic acid sequence shown in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID



NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13,  
SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ  
ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID  
NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29,  
5 SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ  
ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID  
NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45,  
SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ  
ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID  
10 NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61,  
SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ  
ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID  
NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77,  
SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ  
15 ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID  
NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93,  
SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ  
ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID  
NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID  
20 NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID  
NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID  
NO:119, SEQ ID NO:120, and SEQ ID NO:121, or a derivative thereof. Any nucleotide  
or polynucleotide may be used in this regard, provided that its addition, deletion or  
substitution does not alter the amino acid sequence of SEQ ID NO:122, SEQ ID NO:123,  
25 SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128,  
SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133,  
SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138,  
SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143,  
SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148,  
30 SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153,  
SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158,  
SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163,

SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168,  
SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173,  
SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178,  
SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183,  
5 SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188,  
SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193,  
SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198,  
SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203,  
SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208,  
10 SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213,  
SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218,  
SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223,  
SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228,  
SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233,  
15 SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238,  
SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, that is encoded  
by the nucleotide sequence. For example, the present invention is intended to include any  
nucleic acid sequence resulting from the addition of ATG as an initiation codon at the 5'-  
end of the inventive nucleic acid sequence or its derivative, or from the addition of TTA,  
20 TAG or TGA as a termination codon at the 3'-end of the inventive nucleotide sequence or  
its derivative. Moreover, the nucleic acid molecule of the present invention may, as  
necessary, have restriction endonuclease recognition sites added to its 5'-end and/or 3'-  
end.

Such functional alterations of a given nucleic acid sequence afford an opportunity  
25 to promote secretion and/or processing of heterologous proteins encoded by foreign  
nucleic acid sequences fused thereto, for example. All variations of the nucleotide  
sequence of the kinase genes of the invention and fragments thereof permitted by the  
genetic code are, therefore, included in this invention.

Further, it is possible to delete codons or to substitute one or more codons with  
30 codons other than degenerate codons to produce a structurally modified polypeptide, but  
one which has substantially the same utility or activity as the polypeptide produced by the  
unmodified nucleic acid molecule. As recognized in the art, the two polypeptides are

functionally equivalent, as are the two nucleic acid molecules that give rise to their production, even though the differences between the nucleic acid molecules are not related to the degeneracy of the genetic code. This is discussed further in the "Functional Derivatives" section, herein.

5           Finally, many of the nucleic acid molecules of the invention are provided as a partial sequence only (Fig. 2A through 2QQ). However, it is standard for one of ordinary skill in the art to obtain a full-length sequence when provided with a partial sequence. Similarly, when provided with a partial or full-length sequence it is standard for one of ordinary skill in the art to obtain nucleic acid sequence coding for homologous proteins.  
10           Therefore, these nucleic acid molecules are also part of the invention.

          The characteristics of the protein kinase nucleic acid sequences of the invention are provided in Table 1. The protein kinases fall into 10 known groups: AGC, CAMK, CKI, CMGC, dsPK, EIFK, LIMK, MLK, STE and TK. In addition, there are a significant number of protein kinases that do not belong to any of the known groups, and therefore  
15           presumably define new protein kinase groups.

          Additional characteristics may be found, *inter alia*, in the tables, namely Table 1, Table 2, Table 3 and Table 4, shown below.

## 20           II. Nucleic Acid Probes, Methods, and Kits for Detection of Protein Kinases.

          A nucleic acid probe of the present invention may be used to probe an appropriate chromosomal or cDNA library by usual hybridization methods to obtain other nucleic acid molecules of the present invention. A chromosomal DNA or cDNA library may be prepared from appropriate cells according to recognized methods in the art (cf. "Molecular Cloning: A Laboratory Manual", second edition, Cold Spring Harbor Laboratory,  
25           Sambrook, Fritsch, & Maniatis, eds., 1989).

          In the alternative, chemical synthesis can be carried out in order to obtain nucleic acid probes having nucleotide sequences that correspond to N-terminal, kinase or C-terminal portions, for example, of the amino acid sequence of the polypeptide of interest. The synthesized nucleic acid probes may be used as primers in a polymerase chain  
30           reaction (PCR) carried out in accordance with recognized PCR techniques, essentially according to PCR Protocols, "A Guide to Methods and Applications", Academic Press.

Michael, *et al.*, eds., 1990, utilizing the appropriate chromosomal or cDNA library to obtain the fragment of the present invention.

One skilled in the art can readily design such probes based on the sequence disclosed herein using methods of computer alignment and sequence analysis known in the art ("Molecular Cloning: A Laboratory Manual", 1989, *supra*). The hybridization probes of the present invention can be labeled by standard labeling techniques such as with a radiolabel, enzyme label, fluorescent label, biotin-avidin label, chemiluminescence, and the like. After hybridization, the probes may be visualized using known methods.

The nucleic acid probes of the present invention include RNA, as well as DNA probes, such probes being generated using techniques known in the art. The nucleic acid probe may be immobilized on a solid support. Examples of such solid supports include, but are not limited to, plastics such as polycarbonate, complex carbohydrates such as agarose and sepharose, and acrylic resins, such as polyacrylamide and latex beads. Techniques for coupling nucleic acid probes to such solid supports are well known in the art.

The test samples suitable for nucleic acid probing methods of the present invention include, for example, cells or nucleic acid extracts of cells, or biological fluids. The samples used in the above-described methods will vary based on the assay format, the detection method and the nature of the tissues, cells or extracts to be assayed. Methods for preparing nucleic acid extracts of cells are well known in the art and can be readily adapted in order to obtain a sample that is compatible with the method utilized.

One method of detecting the presence of nucleic acids of the invention in a sample comprises (a) contacting said sample with the above-described nucleic acid probe under conditions such that hybridization occurs, and (b) detecting the presence of said probe bound to said nucleic acid molecule. One skilled in the art would select the nucleic acid probe according to techniques known in the art as described above. Samples to be tested include but should not be limited to RNA samples of human tissue.

A kit for detecting the presence of nucleic acids of the invention in a sample comprises at least one container means having disposed therein the above-described nucleic acid probe. The kit may further comprise other containers comprising one or more of the following: wash reagents and reagents capable of detecting the presence of bound nucleic acid probe. Examples of detection reagents include, but are not limited to

radiolabelled probes, enzymatic labeled probes (horseradish peroxidase, alkaline phosphatase), and affinity labeled probes (biotin, avidin, or streptavidin).

In detail, a compartmentalized kit includes any kit in which reagents are contained in separate containers. Such containers include small glass containers, plastic containers or strips of plastic or paper. Such containers allow the efficient transfer of reagents from one compartment to another compartment such that the samples and reagents are not cross-contaminated and the agents or solutions of each container can be added in a quantitative fashion from one compartment to another. Such containers will include a container which will accept the test sample, a container which contains the probe or primers used in the assay, containers which contain wash reagents (such as phosphate buffered saline, Tris-buffers, and the like), and containers which contain the reagents used to detect the hybridized probe, bound antibody, amplified product, or the like. One skilled in the art will readily recognize that the nucleic acid probes described in the present invention can readily be incorporated into one of the established kit formats that are well known in the art.

### III. DNA Constructs Comprising a Protein Kinase Nucleic Acid Molecule and Cells Containing These Constructs.

The present invention also relates to a recombinant DNA molecule comprising, 5' to 3', a promoter effective to initiate transcription in a host cell and the above-described nucleic acid molecules. In addition, the present invention relates to a recombinant DNA molecule comprising a vector and an above-described nucleic acid molecule. The present invention also relates to a nucleic acid molecule comprising a transcriptional region functional in a cell, a sequence complementary to an RNA sequence encoding an amino acid sequence corresponding to the above-described polypeptide, and a transcriptional termination region functional in said cell. The above-described molecules may be isolated and/or purified DNA molecules.

The present invention also relates to a cell or organism that contains an above-described nucleic acid molecule and thereby is capable of expressing a polypeptide. The polypeptide may be purified from cells that have been altered to express the polypeptide. A cell is said to be "altered to express a desired polypeptide" when the cell, through genetic manipulation, is made to produce a protein which it normally does not produce or



which the cell normally produces at lower levels. One skilled in the art can readily adapt procedures for introducing and expressing either genomic, cDNA, or synthetic sequences into either eukaryotic or prokaryotic cells.

5 A nucleic acid molecule, such as DNA, is said to be "capable of expressing" a polypeptide if it contains nucleotide sequences which contain transcriptional and translational regulatory information and such sequences are "operably linked" to nucleotide sequences which encode the polypeptide. An operable linkage is a linkage in which the regulatory DNA sequences and the DNA sequence sought to be expressed are connected in such a way as to permit gene sequence expression. The precise nature of the  
10 regulatory regions needed for gene sequence expression may vary from organism to organism, but shall in general include a promoter region which, in prokaryotes, contains both the promoter (which directs the initiation of RNA transcription) as well as the DNA sequences which, when transcribed into RNA, will signal synthesis initiation. Such regions will normally include those 5'-non-coding sequences involved with initiation of  
15 transcription and translation, such as the TATA box, capping sequence, CAAT sequence, and the like.

If desired, the non-coding region 3' to the sequence encoding a kinase of the invention may be obtained by the above-described methods. This region may be retained for its transcriptional termination regulatory sequences, such as termination and  
20 polyadenylation. Thus, by retaining the 3'-region naturally contiguous to the DNA sequence encoding a kinase of the invention, the transcriptional termination signals may be provided. Where the transcriptional termination signals are not satisfactorily functional in the expression host cell, then a 3' region functional in the host cell may be substituted.

Two DNA sequences (such as a promoter region sequence and a sequence  
25 encoding a kinase of the invention) are said to be operably linked if the nature of the linkage between the two DNA sequences does not (1) result in the introduction of a frame-shift mutation, (2) interfere with the ability of the promoter region sequence to direct the transcription of a gene sequence encoding a kinase of the invention, or (3) interfere with the ability of the gene sequence of a kinase of the invention to be transcribed by the  
30 promoter region sequence. Thus, a promoter region would be operably linked to a DNA sequence if the promoter were capable of effecting transcription of that DNA sequence.

Thus, to express a gene encoding a kinase of the invention, transcriptional and translational signals recognized by an appropriate host are necessary.

The present invention encompasses the expression of a gene encoding a kinase of the invention (or a functional derivative thereof) in either prokaryotic or eukaryotic cells. Prokaryotic hosts are, generally, very efficient and convenient for the production of recombinant proteins and are, therefore, one type of preferred expression system for kinases of the invention. Prokaryotes most frequently are represented by various strains of *E. coli*. However, other microbial strains may also be used, including other bacterial strains.

In prokaryotic systems, plasmid vectors that contain replication sites and control sequences derived from a species compatible with the host may be used. Examples of suitable plasmid vectors may include pBR322, pUC118, pUC119 and the like; suitable phage or bacteriophage vectors may include  $\gamma$ gt10,  $\gamma$ gt11 and the like; and suitable virus vectors may include pMAM-neo, pKRC and the like. Preferably, the selected vector of the present invention has the capacity to replicate in the selected host cell.

Recognized prokaryotic hosts include bacteria such as *E. coli*, *Bacillus*, *Streptomyces*, *Pseudomonas*, *Salmonella*, *Serratia*, and the like. However, under such conditions, the polypeptide will not be glycosylated. The prokaryotic host must be compatible with the replicon and control sequences in the expression plasmid.

To express a kinase of the invention (or a functional derivative thereof) in a prokaryotic cell, it is necessary to operably link the sequence encoding the kinase of the invention to a functional prokaryotic promoter. Such promoters may be either constitutive or, more preferably, regulatable (*i.e.*, inducible or derepressible). Examples of constitutive promoters include the *int* promoter of bacteriophage  $\lambda$ , the *bla* promoter of the  $\beta$ -lactamase gene sequence of pBR322, and the *cat* promoter of the chloramphenicol acetyl transferase gene sequence of pPR325, and the like. Examples of inducible prokaryotic promoters include the major right and left promoters of bacteriophage  $\lambda$  ( $P_L$  and  $P_R$ ), the *trp*, *recA*, *lacZ*, *lacI*, and *gal* promoters of *E. coli*, the  $\alpha$ -amylase (Ulmanen *et al.*, J. Bacteriol. 162:176-182, 1985) and the  $\zeta$ -28-specific promoters of *B. subtilis* (Gilman *et al.*, Gene Sequence 32:11-20, 1984), the promoters of the bacteriophages of *Bacillus* (Gryczan, In: The Molecular Biology of the Bacilli, Academic Press, Inc., NY, 1982), and *Streptomyces* promoters (Ward *et al.*, Mol. Gen. Genet. 203:468-478, 1986). Prokaryotic

promoters are reviewed by Glick (Ind. Microbiol. 1:277-282, 1987), Cienatempo (Biochimie 68:505-516, 1986), and Gottesman (Ann. Rev. Genet. 18:415-442, 1984).

Proper expression in a prokaryotic cell also requires the presence of a ribosome-binding site upstream of the gene sequence-encoding sequence. Such ribosome-binding sites are disclosed, for example, by Gold *et al.* (Ann. Rev. Microbiol. 35:365-404, 1981). The selection of control sequences, expression vectors, transformation methods, and the like, are dependent on the type of host cell used to express the gene. As used herein, "cell", "cell line", and "cell culture" may be used interchangeably and all such designations include progeny. Thus, the words "transformants" or "transformed cells" include the primary subject cell and cultures derived therefrom, without regard to the number of transfers. It is also understood that all progeny may not be precisely identical in DNA content, due to deliberate or inadvertent mutations. However, as defined, mutant progeny have the same functionality as that of the originally transformed cell.

Host cells which may be used in the expression systems of the present invention are not strictly limited, provided that they are suitable for use in the expression of the kinase polypeptide of interest. Suitable hosts may often include eukaryotic cells. Preferred eukaryotic hosts include, for example, yeast, fungi, insect cells, mammalian cells either *in vivo*, or in tissue culture. Mammalian cells which may be useful as hosts include HeLa cells, cells of fibroblast origin such as VERO or CHO-K1, or cells of lymphoid origin and their derivatives. Preferred mammalian host cells include SP2/0 and J558L, as well as neuroblastoma cell lines such as IMR 332, which may provide better capacities for correct post-translational processing.

In addition, plant cells are also available as hosts, and control sequences compatible with plant cells are available, such as the cauliflower mosaic virus 35S and 19S, and nopaline synthase promoter and polyadenylation signal sequences. Another preferred host is an insect cell, for example the *Drosophila* larvae. Using insect cells as hosts, the *Drosophila* alcohol dehydrogenase promoter can be used (Rubin, Science 240:1453-1459, 1988). Alternatively, baculovirus vectors can be engineered to express large amounts of kinases of the invention in insect cells (Jasny, Science 238:1653, 1987; Miller *et al.*, In: Genetic Engineering, Vol. 8, Plenum, Setlow *et al.*, eds., pp. 277-297, 1986).

Any of a series of yeast expression systems can be utilized which incorporate promoter and termination elements from the actively expressed sequences coding for glycolytic enzymes that are produced in large quantities when yeast are grown in mediums rich in glucose. Known glycolytic gene sequences can also provide very efficient transcriptional control signals. Yeast provides substantial advantages in that it can also carry out post-translational modifications. A number of recombinant DNA strategies exist utilizing strong promoter sequences and high copy number plasmids which can be utilized for production of the desired proteins in yeast. Yeast recognizes leader sequences on cloned mammalian genes and secretes peptides bearing leader sequences (*i.e.*, pre-peptides). Several possible vector systems are available for the expression of kinases of the invention in a mammalian host.

A wide variety of transcriptional and translational regulatory sequences may be employed, depending upon the nature of the host. The transcriptional and translational regulatory signals may be derived from viral sources, such as adenovirus, bovine papilloma virus, cytomegalovirus, simian virus, or the like, where the regulatory signals are associated with a particular gene sequence which has a high level of expression. Alternatively, promoters from mammalian expression products, such as actin, collagen, myosin, and the like, may be employed. Transcriptional initiation regulatory signals may be selected which allow for repression or activation, so that expression of the gene sequences can be modulated. Of interest are regulatory signals which are temperature-sensitive so that by varying the temperature, expression can be repressed or initiated, or are subject to chemical (such as metabolite) regulation.

Expression of kinases of the invention in eukaryotic hosts requires the use of eukaryotic regulatory regions. Such regions will, in general, include a promoter region sufficient to direct the initiation of RNA synthesis. Preferred eukaryotic promoters include, for example, the promoter of the mouse metallothionein I gene sequence (Hamer *et al.*, J. Mol. Appl. Gen. 1:273-288, 1982); the TK promoter of Herpes virus (McKnight, Cell 31:355-365, 1982); the SV40 early promoter (Benoist *et al.*, Nature (London) 290:304-31, 1981); and the yeast gal4 gene sequence promoter (Johnston *et al.*, Proc. Natl. Acad. Sci. (USA) 79:6971-6975, 1982; Silver *et al.*, Proc. Natl. Acad. Sci. (USA) 81:5951-5955, 1984).

Translation of eukaryotic mRNA is initiated at the codon that encodes the first methionine. For this reason, it is preferable to ensure that the linkage between a eukaryotic promoter and a DNA sequence which encodes a kinase of the invention (or a functional derivative thereof) does not contain any intervening codons which are capable of encoding a methionine (*i.e.*, AUG). The presence of such codons results either in the formation of a fusion protein (if the AUG codon is in the same reading frame as the kinase of the invention coding sequence) or a frame-shift mutation (if the AUG codon is not in the same reading frame as the kinase of the invention coding sequence).

A nucleic acid molecule encoding a kinase of the invention and an operably linked promoter may be introduced into a recipient prokaryotic or eukaryotic cell either as a nonreplicating DNA or RNA molecule, which may either be a linear molecule or, more preferably, a closed covalent circular molecule. Since such molecules are incapable of autonomous replication, the expression of the gene may occur through the transient expression of the introduced sequence. Alternatively, permanent expression may occur through the integration of the introduced DNA sequence into the host chromosome.

A vector may be employed which is capable of integrating the desired gene sequences into the host cell chromosome. Cells which have stably integrated the introduced DNA into their chromosomes can be selected by also introducing one or more markers which allow for selection of host cells which contain the expression vector. The marker may provide for prototrophy to an auxotrophic host, biocide resistance, *e.g.*, antibiotics, or heavy metals, such as copper, or the like. The selectable marker gene sequence can either be directly linked to the DNA gene sequences to be expressed, or introduced into the same cell by co-transfection. Additional elements may also be needed for optimal synthesis of mRNA. These elements may include splice signals, as well as transcription promoters, enhancers, and termination signals. cDNA expression vectors incorporating such elements include those described by Okayama (Mol. Cell. Biol. 3:280-, 1983).

The introduced nucleic acid molecule can be incorporated into a plasmid or viral vector capable of autonomous replication in the recipient host. Any of a wide variety of vectors may be employed for this purpose. Factors of importance in selecting a particular plasmid or viral vector include: the ease with which recipient cells that contain the vector may be recognized and selected from those recipient cells which do not contain the vector;



the number of copies of the vector which are desired in a particular host; and whether it is desirable to be able to "shuttle" the vector between host cells of different species.

Preferred prokaryotic vectors include plasmids such as those capable of replication in *E. coli* (such as, for example, pBR322, ColEI, pSC101, pACYC 184,  $\pi$ VX; "Molecular Cloning: A Laboratory Manual", 1989, *supra*). *Bacillus* plasmids include pC194, pC221, pT127, and the like (Gryczan, In: The Molecular Biology of the Bacilli, Academic Press, NY, pp. 307-329, 1982). Suitable *Streptomyces* plasmids include pIJ101 (Kendall *et al.*, J. Bacteriol. 169:4177-4183, 1987), and streptomyces bacteriophages such as  $\phi$ C31 (Chater *et al.*, In: Sixth International Symposium on Actinomycetales Biology, Akademiai Kiado, Budapest, Hungary, pp. 45-54, 1986). *Pseudomonas* plasmids are reviewed by John *et al.* (Rev. Infect. Dis. 8:693-704, 1986), and Izaki (Jpn. J. Bacteriol. 33:729-742, 1978).

Preferred eukaryotic plasmids include, for example, BPV, vaccinia, SV40, 2-micron circle, and the like, or their derivatives. Such plasmids are well known in the art (Botstein *et al.*, Miami Wntr. Symp. 19:265-274, 1982; Broach, In: "The Molecular Biology of the Yeast *Saccharomyces*: Life Cycle and Inheritance", Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, p. 445-470, 1981; Broach, Cell 28:203-204, 1982; Bollon *et al.*, J. Clin. Hematol. Oncol. 10:39-48, 1980; Maniatis, In: Cell Biology: A Comprehensive Treatise, Vol. 3, Gene Sequence Expression, Academic Press, NY, pp. 563-608, 1980).

Once the vector or nucleic acid molecule containing the construct(s) has been prepared for expression, the DNA construct(s) may be introduced into an appropriate host cell by any of a variety of suitable means, *i.e.*, transformation, transfection, conjugation, protoplast fusion, electroporation, particle gun technology, calcium phosphate-precipitation, direct microinjection, and the like. After the introduction of the vector, recipient cells are grown in a selective medium, which selects for the growth of vector-containing cells. Expression of the cloned gene(s) results in the production of a kinase of the invention, or fragments thereof. This can take place in the transformed cells as such, or following the induction of these cells to differentiate (for example, by administration of bromodeoxyuracil to neuroblastoma cells or the like). A variety of incubation conditions can be used to form the peptide of the present invention. The most preferred conditions are those which mimic physiological conditions.

#### IV. The Proteins of the Invention

A variety of methodologies known in the art can be utilized to obtain the polypeptides of the present invention. The polypeptides may be purified from tissues or cells that naturally produce the polypeptides. Alternatively, the above-described isolated nucleic acid fragments could be used to express the kinases of the invention in any organism. The samples of the present invention include cells, protein extracts or membrane extracts of cells, or biological fluids. The samples will vary based on the assay format, the detection method, and the nature of the tissues, cells or extracts used as the sample.

Any eukaryotic organism can be used as a source for the polypeptides of the invention, as long as the source organism naturally contains such polypeptides. As used herein, "source organism" refers to the original organism from which the amino acid sequence of the subunit is derived, regardless of the organism the subunit is expressed in and ultimately isolated from.

One skilled in the art can readily follow known methods for isolating proteins in order to obtain the polypeptides free of natural contaminants. These include, but are not limited to: size-exclusion chromatography, HPLC, ion-exchange chromatography, and immuno-affinity chromatography.

Further, the polypeptides of the invention include the full-length polypeptides that can be identified from the full-length or partial sequences encoded by SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182,

SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187,  
SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199,  
SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197,  
SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202,  
5 SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207,  
SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212,  
SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217,  
SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222,  
SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227,  
10 SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232,  
SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237,  
SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID  
NO:242 (Figure 1). In addition, the polypeptides of the invention include the domains of  
these polypeptides, including, but not limited to, the N-terminal, kinase/catalytic, and C-  
15 terminal domains.

The characteristics of the protein kinase nucleic acid sequences of the invention are  
provided in Table 1. The protein kinases fall into 10 known groups: AGC, CAMK, CKI,  
CMGC, dsPK, EIFK, LIMK, MLK, STE and TK. In addition, there are a significant  
number of protein kinases that do not belong to any of the known groups, and therefore  
20 presumably define new protein kinase groups.

Additional characteristics are shown in, *inter alia*, the tables, namely Table 1,  
Table 2, Table 3 and Table 4, provided below.

#### V. Antibodies, Hybridomas, Methods of Use and Kits for Detection of Protein 25 Kinases

The present invention relates to an antibody having binding affinity to a kinase of  
the invention. The polypeptide may have an amino acid sequence selected from the group  
consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ  
ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ  
30 ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ  
ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ  
ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ

ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or a functional derivative thereof, or at least 9 contiguous amino acids thereof (preferably, at least 20, 30, 35, or 40 or more contiguous amino acids thereof). Alternatively, the antibody may bind to a part of the polypeptide not provided in the sequences above, but that is present in the full-length sequence of the polypeptide and that is easily obtained using methods standard in the art. Further, the antibody may bind specifically to particular domains of one or more of the kinases of the invention, including, but not limited to, the N-terminal, kinase/catalytic, or C-terminal domains.

The present invention also relates to an antibody having specific binding affinity to a kinase or kinase domain of the invention. Such an antibody may be isolated by comparing its binding affinity to a kinase of the invention with its binding affinity to other polypeptides. Those that bind selectively to a kinase of the invention would be chosen for use in methods requiring a distinction between a kinase of the invention and other

polypeptides. Such methods could include, but should not be limited to, the analysis of altered kinase expression in tissue containing other polypeptides.

The kinases of the present invention can be used in a variety of procedures and methods, such as for the generation of antibodies, for use in identifying pharmaceutical compositions, and for studying DNA/protein interaction.

The kinases of the present invention can be used to produce antibodies or hybridomas. One skilled in the art will recognize that if an antibody is desired, such a peptide could be generated as described herein and used as an immunogen. The antibodies of the present invention include monoclonal and polyclonal antibodies, as well fragments of these antibodies, and humanized forms. Humanized forms of the antibodies of the present invention may be generated using one of the procedures known in the art such as chimerization or CDR grafting.

The present invention also relates to a hybridoma that produces the above-described monoclonal antibody, or binding fragment thereof. A hybridoma is an immortalized cell line that is capable of secreting a specific monoclonal antibody.

In general, techniques for preparing monoclonal antibodies and hybridomas are well known in the art (Campbell, "Monoclonal Antibody Technology: Laboratory Techniques in Biochemistry and Molecular Biology," Elsevier Science Publishers, Amsterdam, The Netherlands, 1984; St. Groth *et al.*, J. Immunol. Methods 35:1-21, 1980). Any animal (mouse, rabbit, and the like) which is known to produce antibodies can be immunized with the selected polypeptide. Methods for immunization are well known in the art. Such methods include subcutaneous or intraperitoneal injection of the polypeptide. One skilled in the art will recognize that the amount of polypeptide used for immunization will vary based on the animal that is immunized, the antigenicity of the polypeptide and the site of injection.

The polypeptide may be modified or administered in an adjuvant in order to increase the peptide antigenicity. Methods of increasing the antigenicity of a polypeptide are well known in the art. Such procedures include coupling the antigen with a heterologous protein (such as globulin or  $\beta$ -galactosidase) or through the inclusion of an adjuvant during immunization.



For monoclonal antibodies, spleen cells from the immunized animals are removed, fused with myeloma cells, such as SP2'O-Agl4 myeloma cells, and allowed to become monoclonal antibody producing hybridoma cells. Any one of a number of methods well known in the art can be used to identify the hybridoma cell that produces an antibody with the desired characteristics. These include screening the hybridomas with an ELISA assay, western blot analysis, or radioimmunoassay (Lutz *et al.*, Exp. Cell Res. 175:109-124, 1988). Hybridomas secreting the desired antibodies are cloned and the class and subclass are determined using procedures known in the art (Campbell, "Monoclonal Antibody Technology: Laboratory Techniques in Biochemistry and Molecular Biology", *supra*, 1984).

For polyclonal antibodies, antibody-containing antisera is isolated from the immunized animal and is screened for the presence of antibodies with the desired specificity using one of the above-described procedures. The above-described antibodies may be detectably labeled. Antibodies can be detectably labeled through the use of radioisotopes, affinity labels (such as biotin, avidin, and the like), enzymatic labels (such as horse radish peroxidase, alkaline phosphatase, and the like) fluorescent labels (such as FITC or rhodamine, and the like), paramagnetic atoms, and the like. Procedures for accomplishing such labeling are well-known in the art, for example, see Stemberger *et al.*, J. Histochem. Cytochem. 18:315, 1970; Bayer *et al.*, Meth. Enzym. 62:308-, 1979; Engval *et al.*, Immunol. 109:129-, 1972; Goding, J. Immunol. Meth. 13:215-, 1976. The labeled antibodies of the present invention can be used for *in vitro*, *in vivo*, and *in situ* assays to identify cells or tissues that express a specific peptide.

The above-described antibodies may also be immobilized on a solid support. Examples of such solid supports include plastics such as polycarbonate, complex carbohydrates such as agarose and sepharose, acrylic resins and such as polyacrylamide and latex beads. Techniques for coupling antibodies to such solid supports are well known in the art (Weir *et al.*, "Handbook of Experimental Immunology" 4th Ed., Blackwell Scientific Publications, Oxford, England, Chapter 10, 1986; Jacoby *et al.*, Meth. Enzym. 34, Academic Press, N.Y., 1974). The immobilized antibodies of the present invention can be used for *in vitro*, *in vivo*, and *in situ* assays as well as in immunochromatography.

Furthermore, one skilled in the art can readily adapt currently available procedures, as well as the techniques, methods and kits disclosed herein with regard to antibodies, to generate peptides capable of binding to a specific peptide sequence in order to generate rationally designed antipeptide peptides (Hurby *et al.*, "Application of Synthetic Peptides: Antisense Peptides", In Synthetic Peptides, A User's Guide, W.H. Freeman, NY, pp. 289-307, 1992; Kaspczak *et al.*, Biochemistry 28:9230-9238, 1989).

Anti-peptide peptides can be generated by replacing the basic amino acid residues found in the peptide sequences of the kinases of the invention with acidic residues, while maintaining hydrophobic and uncharged polar groups. For example, lysine, arginine, and/or histidine residues are replaced with aspartic acid or glutamic acid and glutamic acid residues are replaced by lysine, arginine or histidine.

The present invention also encompasses a method of detecting a kinase polypeptide in a sample, comprising: (a) contacting the sample with an above-described antibody, under conditions such that immunocomplexes form, and (b) detecting the presence of said antibody bound to the polypeptide. In detail, the methods comprise incubating a test sample with one or more of the antibodies of the present invention and assaying whether the antibody binds to the test sample. Altered levels of a kinase of the invention in a sample as compared to normal levels may indicate disease.

Conditions for incubating an antibody with a test sample vary. Incubation conditions depend on the format employed in the assay, the detection methods employed, and the type and nature of the antibody used in the assay. One skilled in the art will recognize that any one of the commonly available immunological assay formats (such as radioimmunoassays, enzyme-linked immunosorbent assays, diffusion based Ouchterlony, or rocket immunofluorescent assays) can readily be adapted to employ the antibodies of the present invention. Examples of such assays can be found in Chard ("An Introduction to Radioimmunoassay and Related Techniques" Elsevier Science Publishers, Amsterdam, The Netherlands, 1986), Bullock *et al.* ("Techniques in Immunocytochemistry," Academic Press, Orlando, FL Vol. 1, 1982; Vol. 2, 1983; Vol. 3, 1985), Tijssen ("Practice and Theory of Enzyme Immunoassays: Laboratory Techniques in Biochemistry and Molecular Biology," Elsevier Science Publishers, Amsterdam, The Netherlands, 1985).

The immunological assay test samples of the present invention include cells, protein or membrane extracts of cells, or biological fluids such as blood, serum, plasma, or urine. The test samples used in the above-described method will vary based on the assay format, nature of the detection method and the tissues, cells or extracts used as the sample to be assayed. Methods for preparing protein extracts or membrane extracts of cells are well known in the art and can be readily be adapted in order to obtain a sample which is testable with the system utilized.

A kit contains all the necessary reagents to carry out the previously described methods of detection. The kit may comprise: (i) a first container means containing an above-described antibody, and (ii) second container means containing a conjugate comprising a binding partner of the antibody and a label. In another preferred embodiment, the kit further comprises one or more other containers comprising one or more of the following: wash reagents and reagents capable of detecting the presence of bound antibodies.

Examples of detection reagents include, but are not limited to, labeled secondary antibodies, or in the alternative, if the primary antibody is labeled, the chromophoric, enzymatic, or antibody binding reagents that are capable of reacting with the labeled antibody. The compartmentalized kit may be as described above for nucleic acid probe kits. One skilled in the art will readily recognize that the antibodies described in the present invention can readily be incorporated into one of the established kit formats that are well known in the art.

#### VI. Isolation of Compounds That Interact With Protein Kinases

The present invention also relates to a method of detecting a compound capable of binding to a protein kinase of the invention, comprising incubating the compound with a kinase of the invention and detecting the presence of the compound bound to the kinase. The compound may be present within a complex mixture, for example, serum, body fluid, or cell extracts.

The present invention also relates to a method of detecting an agonist or antagonist of kinase activity or kinase binding partner activity comprising incubating cells that produce a kinase of the invention in the presence of a compound and detecting changes in the level of kinase activity or kinase binding partner activity. The compounds thus identified would produce a change in activity indicative of the presence of the compound.

The compound may be present within a complex mixture, for example, serum, body fluid, or cell extracts. Once the compound is identified it can be isolated using techniques well known in the art.

The present invention also encompasses a method of agonizing (stimulating) or antagonizing kinase associated activity in a mammal comprising administering to said mammal an agonist or antagonist to a kinase of the invention in an amount sufficient to effect said agonism or antagonism. A method of treating diseases in a mammal with an agonist or antagonist of kinase activity comprising administering the agonist or antagonist to a mammal in an amount sufficient to agonize or antagonize kinase associated functions is also encompassed in the present application.

In an effort to discover novel treatments for diseases, biomedical researchers and chemists have designed, synthesized, and tested molecules that inhibit the function of protein kinases. Some small organic molecules form a class of compounds that modulate the function of protein kinases. Examples of molecules that have been reported to inhibit the function of protein kinases include, but are not limited to, bis monocyclic, bicyclic or heterocyclic aryl compounds (PCT WO 92/20642, published November 26, 1992 by Maguire *et al.*), vinylene-azaindole derivatives (PCT WO 94/14808, published July 7, 1994 by Ballinari *et al.*), 1-cyclopropyl-4-pyridyl-quinolones (U.S. Patent No. 5,330,992), styryl compounds (U.S. Patent No. 5,217,999), styryl-substituted pyridyl compounds (U.S. Patent No. 5,302,606), certain quinazoline derivatives (EP Application No. 0 566 266 A1), seleoindoles and selenides (PCT WO 94/03427, published February 17, 1994 by Denny *et al.*), tricyclic polyhydroxylic compounds (PCT WO 92/21660, published December 10, 1992 by Dow), and benzylphosphonic acid compounds (PCT WO 91/15495, published October 17, 1991 by Dow *et al.*).

Compounds that can traverse cell membranes and are resistant to acid hydrolysis are potentially advantageous as therapeutics as they can become highly bioavailable after being administered orally to patients. However, many of these protein kinase inhibitors only weakly inhibit the function of protein kinases. In addition, many inhibit a variety of protein kinases and will cause multiple side-effects as therapeutics for diseases.

Some indolinone compounds, however, form classes of acid resistant and membrane permeable organic molecules. WO 96/22976 (published August 1, 1996 by Ballinari *et al.*) describes hydrosoluble indolinone compounds that harbor tetralin,

naphthalene, quinoline, and indole substituents fused to the oxindole ring. These bicyclic substituents are in turn substituted with polar moieties including hydroxylated alkyl, phosphate, and ether moieties. U.S. Patent Application Serial Nos. 08/702,232, filed August 23, 1996, entitled "Indolinone Combinatorial Libraries and Related Products and Methods for the Treatment of Disease" by Tang *et al.* (Lyon & Lyon Docket No. 221/187) and 08/485,323, filed June 7, 1995, entitled "Benzyldiene-Z-Indoline Compounds for the Treatment of Disease" by Tang *et al.* (Lyon & Lyon Docket No. 223/298) and International Patent Publication WO 96/22976, published August 1, 1996 by Ballinari *et al.*, all of which are incorporated herein by reference in their entirety, including any drawings, describe indolinone chemical libraries of indolinone compounds harboring other bicyclic moieties as well as monocyclic moieties fused to the oxindole ring. Applications 08/702,232, filed August 23, 1996, entitled "Indolinone Combinatorial Libraries and Related Products and Methods for the Treatment of Disease" by Tang *et al.* (Lyon & Lyon Docket No. 221/187), 08/485,323, filed June 7, 1995, entitled "Benzyldiene-Z-Indoline Compounds for the Treatment of Disease" by Tang *et al.* (Lyon & Lyon Docket No. 223/298), and WO 96/22976, published August 1, 1996 by Ballinari *et al.* teach methods of indolinone synthesis, methods of testing the biological activity of indolinone compounds in cells, and inhibition patterns of indolinone derivatives.

Other examples of substances capable of modulating kinase activity include, but are not limited to, tyrphostins, quinazolines, quinoxolines, and quinolines. The quinazolines, tyrphostins, quinolines, and quinoxolines referred to above include well known compounds such as those described in the literature. For example, representative publications describing quinazolines include Barker *et al.*, EPO Publication No. 0 520 722 A1; Jones *et al.*, U.S. Patent No. 4,447,608; Kabbe *et al.*, U.S. Patent No. 4,757,072; Kaul and Vougioukas, U.S. Patent No. 5, 316,553; Kreighbaum and Comer, U.S. Patent No. 4,343,940; Pegg and Wardleworth, EPO Publication No. 0 562 734 A1; Barker *et al.*, Proc. of Am. Assoc. for Cancer Research 32:327 (1991); Bertino, J.R., Cancer Research 3:293-304 (1979); Bertino, J.R., Cancer Research 9(2 part 1):293-304 (1979); Curtin *et al.*, Br. J. Cancer 53:361-368 (1986); Fernandes *et al.*, Cancer Research 43:1117-1123 (1983); Ferris *et al.* J. Org. Chem. 44(2):173-178; Fry *et al.*, Science 265:1093-1095 (1994); Jackman *et al.*, Cancer Research 51:5579-5586 (1981); Jones *et al.* J. Med. Chem. 29(6):1114-1118; Lee and Skibo, Biochemistry 26(23):7355-7362 (1987); Lemus *et al.*, J.



Org. Chem. 54:3511-3518 (1989); Ley and Seng, Synthesis 1975:415-522 (1975); Maxwell *et al.*, Magnetic Resonance in Medicine 17:189-196 (1991); Mini *et al.*, Cancer Research 45:325-330 (1985); Phillips and Castle, J. Heterocyclic Chem. 17(19):1489-1596 (1980); Reece *et al.*, Cancer Research 47(11):2996-2999 (1977); Sculier *et al.*, Cancer Immunol. and Immunother. 23:A65 (1986); Sikora *et al.*, Cancer Letters 23:289-295 (1984); Sikora *et al.*, Analytical Biochem. 172:344-355 (1988); all of which are incorporated herein by reference in their entirety, including any drawings.

Quinoxaline is described in Kaul and Vougioukas, U.S. Patent No. 5,316,553, incorporated herein by reference in its entirety, including any drawings.

Quinolines are described in Dolle *et al.*, J. Med. Chem. 37:2627-2629 (1994); MaGuire, J. Med. Chem. 37:2129-2131 (1994); Burke *et al.*, J. Med. Chem. 36:425-432 (1993); and Burke *et al.*, BioOrganic Med. Chem. Letters 2:1771-1774 (1992), all of which are incorporated by reference in their entirety, including any drawings.

Tyrphostins are described in Allen *et al.*, Clin. Exp. Immunol. 91:141-156 (1993); Anafi *et al.*, Blood 82:12:3524-3529 (1993); Baker *et al.*, J. Cell Sci. 102:543-555 (1992); Bilder *et al.*, Amer. Physiol. Soc. pp. 6363-6143:C721-C730 (1991); Brunton *et al.*, Proceedings of Amer. Assoc. Cancer Rsch. 33:558 (1992); Bryckaert *et al.*, Experimental Cell Research 199:255-261 (1992); Dong *et al.*, J. Leukocyte Biology 53:53-60 (1993); Dong *et al.*, J. Immunol. 151(5):2717-2724 (1993); Gazit *et al.*, J. Med. Chem. 32:2344-2352 (1989); Gazit *et al.*, "J. Med. Chem. 36:3556-3564 (1993); Kaur *et al.*, Anti-Cancer Drugs 5:213-222 (1994); Kaur *et al.*, King *et al.*, Biochem. J. 275:413-418 (1991); Kuo *et al.*, Cancer Letters 74:197-202 (1993); Levitzki, A., The FASEB J. 6:3275-3282 (1992); Lyall *et al.*, J. Biol. Chem. 264:14503-14509 (1989); Peterson *et al.*, The Prostate 22:335-345 (1993); Pillemer *et al.*, Int. J. Cancer 50:80-85 (1992); Posner *et al.*, Molecular Pharmacology 45:673-683 (1993); Rendu *et al.*, Biol. Pharmacology 44(5):881-888 (1992); Sauro and Thomas, Life Sciences 53:371-376 (1993); Sauro and Thomas, J. Pharm. and Experimental Therapeutics 267(3):119-1125 (1993); Wolbring *et al.*, J. Biol. Chem. 269(36):22470-22472 (1994); and Yoneda *et al.*, Cancer Research 51:4430-4435 (1991); all of which are incorporated herein by reference in their entirety, including any drawings.

Other compounds that could be used as modulators include oxindolinones such as those described in U.S. patent application Serial No. 08/702,232 filed August 23, 1996, incorporated herein by reference in its entirety, including any drawings.

VII. Biological Significance, Applications and Clinical Relevance of Novel Protein  
5 Kinases

For each protein kinase in this application, we provide a classification of the protein class and family to which it belongs, a summary of non-catalytic protein motifs, a profile of its expression in several hundred tissue and cell sources, and a chromosomal location. This information can be used to suggest potential function, regulation or  
10 therapeutic utility for each of the proteins.

The kinase classification and protein domains often reflect pathways, cellular roles, or mechanisms of up- or down-stream regulation. Also disease-relevant genes often occur in families of related genes. For example if one member of a kinase family functions as an oncogene, a tumor suppressor, or has been found to be disrupted in an immune,  
15 neurologic, cardiovascular, or metabolic disorder, frequently other family members may play a related role.

The expression analysis organizes kinases into groups that are transcriptionally upregulated in tumors and those that are more restricted to specific tumor types such as melanoma or prostate. This analysis also identifies genes that are regulated in a cell cycle  
20 dependent manner, and are therefore likely to be involved in maintaining cell cycle checkpoints, entry, progression, or exit from mitosis, oversee DNA repair, or are involved in cell proliferation and genome stability. Expression data also can identify genes expressed in endothelial sources or other tissues that suggest a role in angiogenesis, thereby implicating them as targets for control of diseases that have an angiogenic  
25 component, such as cancer, endometriosis, retinopathy and macular degeneration, and various ischemic or vascular pathologies. A proteins' role in cell survival can also be suggested based on restricted expression in cells subjected to external stress such as oxidative damage, hypoxia, drugs such as cisplatinum, or irradiation. Metastases-associated genes can be implicated when expression is restricted to invading regions of a  
30 tumor, or is only seen in local or distant metastases compared to the primary tumor, or when a gene is upregulated during cell culture models of invasion, migration, or motility.

Chromosomal location can identify candidate targets for a tumor amplicon or a tumor-suppressor locus. Summaries of prevalent tumor amplicons are available in the literature, and can identify tumor types to experimentally be confirmed to contain amplified copies of a kinase gene which localizes to an adjacent region.

5 Based on these criteria several kinases immediately stand out as being of potential therapeutic relevance. The protein kinases can be divided into the following disease-relevant categories (nucleotide Seq ID #s in parentheses):

Tumor associated: Mok (SEQ ID NO:57), EPK2, AA316804 (SEQ ID NO:11), AA435956 (SEQ ID NO:48), AA278842 (SEQ ID NO:88), AA599286 (SEQ ID NO:89), AA826850 (SEQ ID NO:3), HRI (SEQ ID NO:73), MLK4 AA232253 (SEQ ID NO:82), AA883975 SGK 235 (SEQ ID NO:95), AA311714 (SEQ ID NO:101), MPSK1 (SEQ ID NO:110), R19609 (Seq ID111), AA383293 (SEQ ID NO:26).

Prostate-specific: AA234451 (SEQ ID NO:47), TSK4 (SEQ ID NO:93), RIP4 (SEQ ID NO:84), KIAA0965 (SEQ ID NO:8).

15 Oncogenic or proliferation associated: KIAA0781 (SEQ ID NO:38), AA789239 (SEQ ID NO:52), CCRK (SEQ ID NO:54), CLK4 (SEQ ID NO:55), H85389 (SEQ ID NO:97).

Neuronal restricted: CAMKKB (SEQ ID NO:66)

Hematopoietic expressed: PTK9L (SEQ ID NO:22), DRAK2 (SEQ ID NO:29), AI025291 (SEQ ID NO:94)

20 Angiogenic or endothelial expressed: DRAK1 (SEQ ID NO:31), MAK-V (SEQ ID NO:40), TRAD (SEQ ID NO:44), MOK (SEQ ID NO:57), AA08847 (SEQ ID NO:78), HGP\_66444466 (SEQ ID NO:79), RSK4 (SEQ ID NO:16).

Cell cycle regulated: AA454060 (SEQ ID NO:45), KIAA0999 (Mitotic – SEQ ID NO:32), AA579641 (Mitotic – SEQ ID NO:60), AA305176 (Mitotic – SEQ ID NO:6), AA018361 (S1 phase – SEQ ID NO:100).

#### VIII. Transgenic Animals.

A variety of methods are available for the production of transgenic animals associated with this invention. DNA can be injected into the pronucleus of a fertilized egg before fusion of the male and female pronuclei, or injected into the nucleus of an embryonic cell (*e.g.*, the nucleus of a two-cell embryo) following the initiation of cell division (Brinster *et al.*, Proc. Nat. Acad. Sci. USA 82: 4438-4442, 1985). Embryos can

be infected with viruses, especially retroviruses, modified to carry inorganic-ion receptor nucleotide sequences of the invention.

Pluripotent stem cells derived from the inner cell mass of the embryo and stabilized in culture can be manipulated in culture to incorporate nucleotide sequences of the invention. A transgenic animal can be produced from such cells through implantation into a blastocyst that is implanted into a foster mother and allowed to come to term. Animals suitable for transgenic experiments can be obtained from standard commercial sources such as Charles River (Wilmington, MA), Taconic (Germantown, NY), Harlan Sprague Dawley (Indianapolis, IN), etc.

The procedures for manipulation of the rodent embryo and for microinjection of DNA into the pronucleus of the zygote are well known to those of ordinary skill in the art (Hogan *et al.*, *supra*). Microinjection procedures for fish, amphibian eggs and birds are detailed in Houdebine and Chourrout (Experientia 47: 897-905, 1991). Other procedures for introduction of DNA into tissues of animals are described in U.S. Patent No., 4,945,050 (Sanford *et al.*, July 30, 1990).

By way of example only, to prepare a transgenic mouse, female mice are induced to superovulate. Females are placed with males, and the mated females are sacrificed by CO<sub>2</sub> asphyxiation or cervical dislocation and embryos are recovered from excised oviducts. Surrounding cumulus cells are removed. Pronuclear embryos are then washed and stored until the time of injection. Randomly cycling adult female mice are paired with vasectomized males. Recipient females are mated at the same time as donor females. Embryos then are transferred surgically. The procedure for generating transgenic rats is similar to that of mice (Hammer *et al.*, Cell 63:1099-1112, 1990).

Methods for the culturing of embryonic stem (ES) cells and the subsequent production of transgenic animals by the introduction of DNA into ES cells using methods such as electroporation, calcium phosphate/DNA precipitation and direct injection also are well known to those of ordinary skill in the art (Teratocarcinomas and Embryonic Stem Cells, A Practical Approach, E.J. Robertson, ed., IRL Press, 1987).

In cases involving random gene integration, a clone containing the sequence(s) of the invention is co-transfected with a gene encoding resistance. Alternatively, the gene encoding neomycin resistance is physically linked to the sequence(s) of the invention.

Transfection and isolation of desired clones are carried out by any one of several methods well known to those of ordinary skill in the art (E.J. Robertson, *supra*).

DNA molecules introduced into ES cells can also be integrated into the chromosome through the process of homologous recombination (Capecchi, Science 244: 1288-1292, 1989). Methods for positive selection of the recombination event (*i.e.*, neo resistance) and dual positive-negative selection (*i.e.*, neo resistance and gancyclovir resistance) and the subsequent identification of the desired clones by PCR have been described by Capecchi, *supra* and Joyner *et al.* (Nature 338: 153-156, 1989), the teachings of which are incorporated herein in their entirety including any drawings. The final phase of the procedure is to inject targeted ES cells into blastocysts and to transfer the blastocysts into pseudopregnant females. The resulting chimeric animals are bred and the offspring are analyzed by Southern blotting to identify individuals that carry the transgene. Procedures for the production of non-rodent mammals and other animals have been discussed by others (Houdebine and Chourrout, *supra*; Pursel *et al.*, Science 244:1281-1288, 1989; and Simms *et al.*, Bio/Technology 6:179-183, 1988).

Thus, the invention provides transgenic, nonhuman mammals containing a transgene encoding a kinase of the invention or a gene effecting the expression of the kinase. Such transgenic nonhuman mammals are particularly useful as an *in vivo* test system for studying the effects of introduction of a kinase, or regulating the expression of a kinase (*i.e.*, through the introduction of additional genes, antisense nucleic acids, or ribozymes).

A "transgenic animal" is an animal having cells that contain DNA which has been artificially inserted into a cell, which DNA becomes part of the genome of the animal which develops from that cell. Preferred transgenic animals are primates, mice, rats, cows, pigs, horses, goats, sheep, dogs and cats. The transgenic DNA may encode human STE20-related kinases. Native expression in an animal may be reduced by providing an amount of anti-sense RNA or DNA effective to reduce expression of the receptor.

#### IX. Gene Therapy

Protein kinases of the invention, or their genetic sequences will also be useful in gene therapy (reviewed in Miller, Nature 357:455-460, 1992). Miller states that advances have resulted in practical approaches to human gene therapy that have demonstrated



positive initial results. The basic science of gene therapy is described in Mulligan (Science 260:926-931, 1993).

In one preferred embodiment, an expression vector containing protein kinase coding sequence is inserted into cells, the cells are grown *in vitro*, and then are infused in large numbers into patients. In another preferred embodiment, a DNA segment containing a promoter of choice (for example a strong promoter) is transferred into cells containing an endogenous gene encoding kinases of the invention in such a manner that the promoter segment enhances expression of the endogenous kinase gene (for example, the promoter segment is transferred to the cell such that it becomes directly linked to the endogenous kinase gene).

The gene therapy may involve the use of an adenovirus containing kinase cDNA targeted to a tumor, systemic kinase increase by implantation of engineered cells, injection with kinase-encoding virus, or injection of naked kinase DNA into appropriate tissues.

Target cell populations may be modified by introducing altered forms of one or more components of the protein complexes in order to modulate the activity of such complexes. For example, by reducing or inhibiting a complex component activity within target cells, an abnormal signal transduction event(s) leading to a condition may be decreased, inhibited, or reversed. Deletion or missense mutants of a component, that retain the ability to interact with other components of the protein complexes but cannot function in signal transduction may be used to inhibit an abnormal, deleterious signal transduction event.

Expression vectors derived from viruses such as retroviruses, vaccinia virus, adenovirus, adeno-associated virus, herpes viruses, several RNA viruses, or bovine papilloma virus, may be used for delivery of nucleotide sequences (*e.g.*, cDNA) encoding recombinant kinase of the invention protein into the targeted cell population (*e.g.*, tumor cells). Methods which are well known to those skilled in the art can be used to construct recombinant viral vectors containing coding sequences (Maniatis *et al.*, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, N.Y., 1989; Ausubel *et al.*, Current Protocols in Molecular Biology, Greene Publishing Associates and Wiley Interscience, N.Y., 1989). Alternatively, recombinant nucleic acid molecules encoding protein sequences can be used as naked DNA or in a reconstituted system *e.g.*, liposomes or other lipid systems for delivery to target cells (*e.g.*, Felgner *et al.*, Nature 337:387-8,

1989). Several other methods for the direct transfer of plasmid DNA into cells exist for use in human gene therapy and involve targeting the DNA to receptors on cells by complexing the plasmid DNA to proteins (Miller, *supra*).

In its simplest form, gene transfer can be performed by simply injecting minute amounts of DNA into the nucleus of a cell, through a process of microinjection (Capecchi, Cell 22:479-88, 1980). Once recombinant genes are introduced into a cell, they can be recognized by the cell's normal mechanisms for transcription and translation, and a gene product will be expressed. Other methods have also been attempted for introducing DNA into larger numbers of cells. These methods include: transfection, wherein DNA is precipitated with  $\text{CaPO}_4$  and taken into cells by pinocytosis (Chen *et al.*, Mol. Cell Biol. 7:2745-52, 1987); electroporation, wherein cells are exposed to large voltage pulses to introduce holes into the membrane (Chu *et al.*, Nucleic Acids Res. 15:1311-26, 1987); lipofection/liposome fusion, wherein DNA is packaged into lipophilic vesicles which fuse with a target cell (Felgner *et al.*, Proc. Natl. Acad. Sci. USA. 84:7413-7417, 1987); and particle bombardment using DNA bound to small projectiles (Yang *et al.*, Proc. Natl. Acad. Sci. 87:9568-9572, 1990). Another method for introducing DNA into cells is to couple the DNA to chemically modified proteins.

It has also been shown that adenovirus proteins are capable of destabilizing endosomes and enhancing the uptake of DNA into cells. The admixture of adenovirus to solutions containing DNA complexes, or the binding of DNA to polylysine covalently attached to adenovirus using protein crosslinking agents substantially improves the uptake and expression of the recombinant gene (Curiel *et al.*, Am. J. Respir. Cell. Mol. Biol., 6:247-52, 1992).

As used herein "gene transfer" means the process of introducing a foreign nucleic acid molecule into a cell. Gene transfer is commonly performed to enable the expression of a particular product encoded by the gene. The product may include a protein, polypeptide, anti-sense DNA or RNA, or enzymatically active RNA. Gene transfer can be performed in cultured cells or by direct administration into animals. Generally gene transfer involves the process of nucleic acid contact with a target cell by non-specific or receptor mediated interactions, uptake of nucleic acid into the cell through the membrane or by endocytosis, and release of nucleic acid into the cytoplasm from the plasma membrane or endosome. Expression may require, in addition, movement of the nucleic

acid into the nucleus of the cell and binding to appropriate nuclear factors for transcription.

As used herein "gene therapy" is a form of gene transfer and is included within the definition of gene transfer as used herein and specifically refers to gene transfer to express a therapeutic product from a cell *in vivo* or *in vitro*. Gene transfer can be performed *ex vivo* on cells which are then transplanted into a patient, or can be performed by direct administration of the nucleic acid or nucleic acid-protein complex into the patient.

In another preferred embodiment, a vector having nucleic acid sequences encoding a protein kinase polypeptide of the invention is provided in which the nucleic acid sequence is expressed only in specific tissue. Methods of achieving tissue-specific gene expression are set forth in International Publication No. WO 93/09236, filed November 3, 1992 and published May 13, 1993.

In all of the preceding vectors set forth above, a further aspect of the invention is that the nucleic acid sequence contained in the vector may include additions, deletions or modifications to some or all of the sequence of the nucleic acid, as defined above.

In another preferred embodiment, a method of gene replacement is set forth.

"Gene replacement" as used herein means supplying a nucleic acid sequence which is capable of being expressed *in vivo* in an animal and thereby providing or augmenting the function of an endogenous gene that is missing or defective in the animal.

#### X. Administration of Substances

Methods of determining the dosages of compounds to be administered to a patient and modes of administering compounds to an organism are disclosed in U.S. Application Serial No. 08/702,282, filed August 23, 1996 and International patent publication number WO 96/22976, published August 1 1996, both of which are incorporated herein by reference in their entirety, including any drawings, figures, or tables. Those skilled in the art will appreciate that such descriptions are applicable to the present invention and can be easily adapted to it.

The proper dosage depends on various factors such as the type of disease being treated, the particular composition being used, and the size and physiological condition of the patient. Therapeutically effective doses for the compounds described herein can be estimated initially from cell culture and animal models. For example, a dose can be formulated in animal models to achieve a circulating concentration range that initially

takes into account the  $IC_{50}$  as determined in cell culture assays. The animal model data can be used to more accurately determine useful doses in humans.

Plasma half-life and biodistribution of the drug and metabolites in the plasma, tumors, and major organs can be also be determined to facilitate the selection of drugs most appropriate to inhibit a disorder. Such measurements can be carried out. For example, HPLC analysis can be performed on the plasma of animals treated with the drug and the location of radiolabeled compounds can be determined using detection methods such as X-ray, CAT scan, and MRI. Compounds that show potent inhibitory activity in the screening assays, but have poor pharmacokinetic characteristics, can be optimized by altering the chemical structure and retesting. In this regard, compounds displaying good pharmacokinetic characteristics can be used as a model.

Toxicity studies can also be carried out by measuring the blood cell composition. For example, toxicity studies can be carried out in a suitable animal model as follows: 1) the compound is administered to mice (an untreated control mouse should also be used); 2) blood samples are periodically obtained via the tail vein from one mouse in each treatment group; and 3) the samples are analyzed for red and white blood cell counts, blood cell composition, and the percent of lymphocytes versus polymorphonuclear cells. A comparison of results for each dosing regime with the controls indicates if toxicity is present.

At the termination of each toxicity study, further studies can be carried out by sacrificing the animals (preferably, in accordance with the American Veterinary Medical Association guidelines Report of the American Veterinary Medical Assoc. Panel on Euthanasia, *Journal of American Veterinary Medical Assoc.*, 202:229-249, 1993). Representative animals from each treatment group can then be examined by gross necropsy for immediate evidence of metastasis, unusual illness, or toxicity. Gross abnormalities in tissue are noted, and tissues are examined histologically. Compounds causing a reduction in body weight or blood components are less preferred, as are compounds having an adverse effect on major organs. In general, the greater the adverse effect the less preferred the compound.

For the treatment of cancers the expected daily dose of a hydrophobic pharmaceutical agent is between 1 to 500 mg/day, preferably 1 to 250 mg/day, and most preferably 1 to 50 mg/day. Drugs can be delivered less frequently provided plasma levels of the active moiety are sufficient to maintain therapeutic effectiveness.

5 Plasma levels should reflect the potency of the drug. Generally, the more potent the compound the lower the plasma levels necessary to achieve efficacy.

### EXAMPLES

10 The examples below are not limiting and are merely representative of various aspects and features of the present invention. The examples below demonstrate the isolation and characterization of the protein kinases of the invention.

15 EXAMPLE 1: Isolation of cDNA clones Encoding Novel Mammalian Protein Kinases  
Materials and Methods Identification from cDNA databases and isolation of clones  
encoding novel protein kinases

Novel kinases were identified from the public EST databases using a Hidden Markov model, abbreviated HMM (Krogh, A., Brown, M., Mian, I. S., Sjolander, K., and Haussler, D. 1994. Hidden Markov models in computational biology: Applications to protein modeling. *J. Mol. Biol.*, 235:1501-1531). The model was built with 70 mammalian and yeast kinase catalytic domain sequences. These sequences were chosen from a comprehensive collection of kinases such that no two sequences had more than 50% sequence identity. ESTs were translated in six open reading frames and were searched against the model. ESTs that had a score of at least 10 against the HMM were then masked for repetitive sequences and vectors and were clustered using MSA. The resulting contigs were searched against known kinases to identify EST clones that encode novel kinases.

25 Approximately 40% of the ESTs encoding potentially novel kinases did not correspond to the correct EST upon sequence analysis. Most of these discrepancies were resolved by ordering additional clones, however, 14 remained unavailable. These 14 ESTs were amplified from a variety of single-stranded cDNA sources with primers derived from the corresponding EST entry as shown on Table 5. The PCR product was subcloned into a bluescript vector, digested to confirm the presence of a correct size insert and sequenced. Full sequencing of EST and PCR was carried out using a cycle sequencing Big-dye kit



with AmpliTaq DNA Polymerase, FS (ABI, Foster City, CA). Sequencing reaction products were run on an ABI Prism 377 DNA Sequencer.

Table 5: Primers used to clone PCR products corresponding to novel kinases

	ID#	ID#	Parent	5' primer	3' primer
sp	na	aa	Sequence	Sequence*	Sequence*
H	33	153	2R22-5-11	GAGATCGRNTTYAARGA RTTYGA	TGTCACNCCNAGNSWCCAN AYRTT
M	81	200	5R57_10_2_ m TESK2_m	GCTGCTGGACAGTGACT TGTATTT	GAAAGCAAAGCCTTACAC CTT
H	67	187	5R69_17_2_h	CTCTCACCTCAGGAAGT GG	GCTTGCGGATCTTCTCA
H	46	166	SGK309_h	GACATCCTGCCGGCCAA CTACG	CGGCCCTGGAGCTGCATCA CTA
M	67	228	5R72_16_2_h	TGCGCGACACCATTGAC CAG	CTCAGGGCTTACATACAGA G
H	45	165	5R72_8_2_h	AAAGGAGAACTACATTT TGAAAAT	CTTCATCATCTCTAATACAT TGGTTGG
H	41	161	Z36720	CAAATTAAGATCATTGA CTTTGGG	GGAAACAAAGTCCTTGGCC TC
H	115	234	AL031652 - Pak6	GTGGACATCTGGTCCCT CG	GTAGGTCCTTCACTCTTGG AG

- degenerate oligonucleotide residue designation:

5 N= A,C,G or T

R= A or G

Y= C or T

S = C or G

W= A or T

10

#### Full-length sequence extension of protein kinases using cDNA and genomic databases

Extension of partial cDNA sequences to encompass the full-length open-reading frame was carried out by iterative blastn searching of the cDNA databases listed in Table 6. All blastn searches were conducted using a blosum62 matrix, a penalty for a nucleotide mismatch of -3 and reward for a nucleotide match of 1. The gapped blast algorithm is described in: (Altschul, Stephen F., Thomas L. Madden, Alejandro A. Schaffer, Jinghui Zhang, Zheng Zhang, Webb Miller, and David J. Lipman (1997), "Gapped BLAST and

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PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Res 25:3389-3402).

Table 6. Databases used for cDNA-based sequence extensions

Database	Database Date
LifeGold templates	Feb 2000
LifeGold compseqs	Feb 2000
LifeGold compseqs	Mar 2000
LifeGold compseqs	Apr 2000
LifeGold fl	Feb 2000
LifeGold flt	Apr 2000
NCBI human Ests	May 2000
NCBI murine Ests	May 2000
NCBI nonredundant	May 2000

5

Extension of partial cDNA sequences to encompass the full-length open-reading frame was also carried out by iterative searches of genomic databases. Three methods were used. The first method made use of the Smith-Waterman algorithm to carry out protein-protein searches of the closest homologue or orthologue to the partial kinase. The target databases consisted of Genescan and open-reading frame (ORF) predictions of all human genomic sequence derived from the human genome project (HGP) as well as from Celera. The complete set of genomic databases searched is shown in Table 7 below. Genomic sequences encoding potential extensions were further assessed by blastp analysis against the NCBI nonredundant to confirm the novelty of the hit. The extending genomic sequences were incorporated into the cDNA sequence after removal of potential introns using the Seqman program from DNASTar. The default parameters used for Smith-Waterman searches were as shown next. Matrix: blosum 62; gap-opening penalty: 12; gap extension penalty: 2. Genescan predictions were made using the Genescan program as detailed in (Chris Burge and Sam Karlin "Prediction of Complete Gene Structures in Human Genomic DNA", JMB (1997) 268(1):78-94). ORF predictions from genomic DNA were made using a standard 6-frame translation.

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The second method for genomic sequence-based extensions made use of tBlastn searches of the homologue or orthologue to the partial kinase against the cDNA databases listed in Table 7. The recognition of significant hits in these databases made possible to identify bridging partial cDNA clones. The iterative application of the two methods made possible the assemblage of the virtual full-length sequence for a large number of the kinases presented in this application. All tblastn searches were conducted using a blosum62 matrix, a penalty for a nucleotide mismatch of -3 and reward for a nucleotide match of 1.

The last method for defining cDNA extensions from genomic sequence used iterative searches of genomic databases through the Genescan program to predict exon splicing and the Genewise program (<http://www.sanger.ac.uk/Software/Wise2/>) to predict potential ORFs based on homology to the closest orthologue/homologue.

Table 7. Databases used for genomic-based sequence extensions

Database	Number of entries	Database Date
Celera v. 1-5	5,306,158	Jan 19/00
Celera v. 6-10	4,209,980	Mar 24/00
Celera v. 11-14	7,222,425	Apr 24/00
Celera v. 15	243,044	May 14/00
HGP all Genescan	25,885	Apr 04/00
HGP; Phase 0	4,944	May 04/00
HGP; Phase 1	28,478	May 05/00
HGP; Phase 2	1,508	May 04/00
HGP; Phase 3	9,971	May 05/00

### Virtual Extensions

Human AA826850 (SEQ ID NO: 3, SEQ ID NO:124)

Blastn analysis of the partial AA826850 sequence revealed an extension to encompass the complete ORF in the Incyte EST 238299.1. A frame-shift correction at position 595 of this EST (marked by X in NA sequence) generated an uninterrupted ORF.

Human AA960957 (SEQ ID NO: 4, SEQ ID NO:125)

Since the initial filing of this application, the partial AA960957 sequence appeared in the public database as the full-length gene for a protein kinase encoded by a gene that maps adjacent to the *evc* (AJ250839) (ellis-van creveld syndrome and weyers acrodermal dysostosis) gene from 4p16.1.

5 Human 5R79-46-1\_h (SEQ ID NO: 5, SEQ ID NO:126)

Blastn analysis of the partial 5R79-46-1 sequence revealed an extension to encompass the complete ORF in the Incyte EST 463894.6. Since the initial filing of this application, the full-length virtual 5R79-46-1 appeared in the public database as the full-length gene for the TANK-binding kinase (TBK1) (Pomerantz, J.L. and Baltimore, D.  
10 (1999) EMBO J. 18 (23), 6694-6704). TBK1 participates in NF- $\kappa$ B activation through the formation of a signaling complex with TRAF2 and TANK.

Human AA305176 (SEQ ID NO: 6, SEQ ID NO:127)

Blastn analysis of the partial AA305176 sequence revealed an extension to encompass the complete ORF in the Incyte EST 220937.1.

15 Human AA256100 (SEQ ID NO: 8, SEQ ID NO:129)

Blastn analysis of the partial AA256100 sequence revealed an extension to encompass the complete ORF through the assembly of three partial clones: Incyte EST 480815.6, KIAA0965 (BAA76809) and AA256100.

Human AA210825 (SEQ ID NO: 9, SEQ ID NO: 130)

20 Blastn analysis of the partial AA210825 sequence revealed an extension to encompass the nearly complete ORF through the assembly of three partial clones: Incyte EST 014721.7, and the NCBI EST's AW01158 and AA210825. An insertion of two "N's" at positions 1915 and 1916 generated an uninterrupted ORF. Blastx analysis indicated the possibility of a start Met in the range of 400-450 nucleotides (i.e. compared to the closest  
25 homolog, human PKCmu (CAA53384.1). However, no Met was found in this region; rather ORF ends in an in-frame stop preceeded by the sequence "RGL LAPGDPPCPPNPAPATPPSSRLPTELF SNFCDS". It is possible that part of the sequence covered by nucleotide positions 1-400 derived from AW01158 comes from an intron, explaining the absence of a start Met.

30 Human AA127299 (SEQ ID NO:10, SEQ ID NO:131)

No entries in the database extended this sequence. The 1684 bp insert of this EST contains a 1369 bp intron at the 3' end. Blastx and SW analysis of the 315 bp coding

region revealed homology to the extracatalytic C2 domain of PKC. This EST, may or may not encode a kinase.

Human AA316804 (SEQ ID NO:11, SEQ ID NO:132)

Since the initial filing of this application, the partial AA316804 sequence appeared in the public database as the full-length gene for the PKC family protein kinase EPK2 or PKCnu (AB015982).

Human H19102 (SEQ ID NO:14, SEQ ID NO:135)

Genewise and Genescan analyses of the partial H19102 sequence revealed an extension from the HGP phase 3 contig 3810672 to encompass the complete catalytic domain of this EST. Blastn analysis against the non-redundant database revealed that this gene is found in the cosmid AC005726 from chromosome 17. H19102 may encode a dual catalytic kinase given the homology to S6 kinase. Analysis of genomic sequence upstream of the 5' end of H19102 revealed a non-kinase gene oriented in the same polarity as H19102 suggestive of the start Met for H19102 being close to the 5' end of the H19102 sequence. From this analysis it is deduced that the second catalytic domain of H19102, if present, is most likely located within the 47334-185,215 bp region of the genomic sequence of AC005726.

Human AA476563 (SEQ ID NO:15, SEQ ID NO:136)

Since the initial filing of this application, the partial AA476563 sequence appeared in the public database as the full-length gene for the protein kinase RPS6KC1 (NM\_012424) (Zhang, H. et al Genomics (1999) 61, 314-318), which is an S6 kinase mapping to 12q12-q13.1.

Human AA626690 (SEQ ID NO:16, SEQ ID NO:137)

Since the initial filing of this application, the partial AA626690 sequence appeared in the public database as the full-length gene for the protein kinase RPS6KA6 (AF184965) (Yntema, H.G et al (1999) Genomics 62, 332-343), an S6 kinase commonly deleted in patients with complex X-linked (Xq21.1 ) mental retardation.

Human AI215680 (SEQ ID NO: 17, SEQ ID NO:138)

Since the initial filing of this application, the partial AI215680 sequence appeared in the public database as the full-length gene encoding a hypothetical protein (AAD30182) from the locus AC006530.4 from chromosome 14.

Human AA887783 (SEQ ID NO:21, SEQ ID NO:142)



Blastn analysis of the partial AA887783 sequence revealed an extension to encompass the nearly complete ORF through the assembly of three partial clones: Incyte 415390R6 and the NCBI EST's AA887783 and N94726. Since the initial filing of this application, the nearly full-length virtual AA887783 sequence appeared in the public database as the full-length gene encoding SGK3 (AF169035), a serum- and glucocorticoid-induced protein kinase (Kobayashi, T. et al (1999) Biochemical J. 344, 189-197.

Human R47805 (SEQ ID NO:22, SEQ ID NO:143)

A cDNA clone encoding the full-length ORF of R47805 was isolated using R47805 as a screening probe. A full-length form for R47805 has also appeared in the public database as

PTK9L (NM\_007284), an A6-related protein kinase.

Human H60215 (SEQ ID NO:23, SEQ ID NO:144)

Blastn analysis of the partial H60215 sequence revealed an extension to encompass the complete ORF in the public EST AI275726. This was confirmed through the full insert sequencing of this EST (2,310 bp) which corresponds to the sequence under SEQ ID NO:144.

A different stop codon was predicted for AI275726 compared to H60215 due to a single nucleotide insertion at position 1586 in AI275726. Evidence for the extra nucleotide comes from EST AI191922.

SGK324\_h orthologue of W30246\_m (SEQ ID NO:24, SEQ ID NO:145)

Blastn, blastx and Smith-Waterman analyses of genomic databases revealed an extension to encompass the complete ORF corresponding to the human orthologue of murine W30246. Exons predicted from the following sequences were used for contig construction: Celera 17000189645083, 17000057549105 and 11000501939981; Incyte142404.1, HGP\_7249119, Incyte 7196489H1, Celera 11000501939981, 17000028165594; Incyte 7249119\_3, Celera 17000035772368, 11000502081575 and 17000140274329. The latter Celera sequence provides the N-terminus.

Human AA383293 (SEQ ID NO:26, SEQ ID NO:147)

Blastn, blastx and Smith-Waterman analyses of genomic databases revealed an extension to encompass the complete ORF corresponding for AA383293. Exons predicted from the following sequences were used for contig construction: (numbers in parenthesis

refer to the aa sequence of the closest homolog (RU2S, NP\_057440) used for the Smith-Waterman query): N-term from Incyte 6010175\_2 (14-97), Incyte 6981981 (134-184) 7596749 (186-232) Celera 17000020789545 (243-301) CAB75619.1 (310-341)--(56-145 DCX homology) 6010175\_2, Celera 17000030058129 (241-262 DCX homology).

5 Human AA021445 (SEQ ID NO:32, SEQ ID NO:152)

Blastn analysis revealed an extension to encompass the nearly complete ORF corresponding for AA021445. Contig reconstruction was as follows: nucleotides 1-802 from KIAA0999 (AB023216); nucleotides 803-4321 from full-insert sequence of AA021445. A pairwise alignment between the AA021445 and KIAA0999 revealed three  
10 inserts in the extracatalytic C-terminus of 48, 48 and 161 aminoacids. In addition, both AA021445 and KIAA0999 have 15 copies of a CAG repeat. Trinucleotide repeats are often found in genes that linked to neurodegenerative diseases.

Human 2R22-55-1 (SEQ ID NO:33, SEQ ID NO:153)

Blastn analysis revealed an extension in the Incyte EST clone 321074.1 to  
15 encompass the complete ORF corresponding to 2R22-55-1.

Human orthologue of AA544838\_m (SEQ ID NO:36, SEQ ID NO:156)

tBlastn analysis identified the partial human KIAA0135 (U79240) clone as the human orthologue of murine AA544838. Blastn revealed an extension KIAA0135\_h (U79240) to encompass the complete ORF. The full ORF was reconstructed from  
20 Incyte406786.5, KFZp430051 and KIAA0135 (U79240).

Human orthologue of AI785735\_m (SEQ ID NO:38, SEQ ID NO:158)

tBlastn analysis identified the partial human KIAA0781 (AB018324) clone as the human orthologue of murine AI785735. Blastn revealed an extension KIAA0135\_h (U79240) to encompass the complete ORF. The full ORF was reconstructed from Incyte  
25 986123.37 KIAA0781 (AB018324).

Human AA207220 (SEQ ID NO: 39, SEQ ID NO:159)

Blastn analysis revealed an extension to encompass the nearly complete ORF corresponding for AA021445. The full ORF was reconstructed from Incyte 402740.1 and AA207220. Frame corrections: deletion of 441 and 595 over Inc402740.1 seq based on  
30 blastx to keep frame open; two n insertions 940, 941 over AA207220 to keep frame open.

Human AA426580 (SEQ ID NO:40, SEQ ID NO:160)

Since the initial filing of this application, the partial AA426580 sequence appeared in the public database as the full-length gene encoding MAK-V (AJ271722) from chromosome 21q22.1.

Human 5R79-54-1 (SEQ ID NO: 41, SEQ ID NO:161)

Genewise and Genescan analyses of the partial 5R79-54-1 sequence revealed an extension from genomic sequence to encode the full ORF for 5R79-54-1.

Human orthologue of AA542015\_m (SEQ ID NO: 42, SEQ ID NO:162)

tBlastn analysis identified KIAA1297 (AB037718). Blastn extended the KIAA1297 sequence to provide the C-terminus through the Incyte 224074.1 EST. The partial ORF consists of a dual catalytic domain flanked by 6 Ig domains and 2 fibronectin repeats. Based on homology to the bt drosophila protein (AAF59316.1), the human form of AA542015 is expected to be missing 16 Ig domains.

Human R19772 (SEQ ID NO:44, SEQ ID NO:164)

The full-length ORF for R19772 was isolated by screening a cDNA library using a probe derived from R19772. Since the initial filing of this application, the R19772 sequence appeared in the public database as the full-length gene encoding Trio (Duet) (AB011422). CDNA library screening revealed multiple isoforms for this gene which are summarized in the Table below.

Table 8. Isoforms for R19772

Kestrl Name	Kestrl AA Acc #	Isoform type	Source	Description*
Trad (Duet)	R19772	B	Skeletal muscle	Deletion of K at 124
				Deletion of Q at 616
				Substitution of E for G at 762
		C	Skeletal muscle	Deletion of K at 124
				Deletion of Q at 616
				Substitution of E for G at 762

				Deletion of 32 aa (160-191)
		D	Lung tumor	Deletion of Q at 616
				Deletion of 32 aa (160-191)
		E	Lung tumor	Deletion of Q at 616
				Deletion of 32 aa (160-191)

\* reference amino acid position are with respect to sequence of Trad (AB011422)

Human AA435956 (SEQ ID NO:48, SEQ ID NO:168)

5        Blastn analysis revealed an extension to encompass the nearly complete catalytic region of AA435956. 5' end sequence extension was provided by genomic locus AC007242.3\_h (range 44880-43801). Based on blastx analysis, the extended sequence encodes is full-length at the C-terminus.

Human AA397553 (SEQ ID NO: 51, SEQ ID NO:171)

10        Since the initial filing of this application, the partial AA397553 sequence appeared in the public database as the full-length gene encoding CRK7 (AF227198), a novel CDC2-related protein kinase that colocalizes with interchromatin granule clusters.

Human AA789239 (SEQ ID NO: 52, SEQ ID NO:172)

15        Since the initial filing of this application, the partial AA789239 sequence appeared in the public database as the full-length gene encoding NKIAMRE (AF130372), a novel kinase deleted in human leukemia.

Human AA631990 (SEQ ID NO:55, SEQ ID NO:175)

20        Blastn analysis revealed an extension to encompass the full-length ORF for AA631990. The full ORF was reconstructed from 253847.5 and AA631990 and AA207220. Frame corrections: delete 1 C at 1380, delete 2N's at 2033/2034.

Human AA557536 (SEQ ID NO:56, SEQ ID NO:176)

25        Blastn analysis revealed an extension to encompass full-length ORF for AA557536. The full ORF was reconstructed from AA557536, celera 11000504061899 and the Incyte 097089.1 EST. An 85bp intron was removed from AA557536.

Human N34132 (SEQ ID NO: 63, SEQ ID NO:183)

Full sequencing of EST N34132 (1.3 kb) confirmed that this cDNA encodes a novel NEK-subfamily kinase. Blast analysis against the EST database showed that four

EST sequences (AA283140, AA283140, AA282911 and N53011) extended the sequence of N34132 at the 3' end to form a 2.31 kb contig. Blast analysis of the new contig against the nonredundant public database showed that the N34132 extended contig overlapped (100% identity) over 228 bp at its 3' end with human KIAA0344 (AB002342), a 5,787 bp cDNA encoding a 1246 aa polypeptide. The 5' 790 bp of the KIAA0344 cDNA (encoding the 58 N-terminal protein sequence) were found to be divergent with respect to the extended 2.32 kb N34132 contig. Evidence that the extended N34132 contig (2.31kb) and KIAA0344 (AB002342) belong to the same gene is the following. First, blast analysis of the nucleotide sequences for N34132 and KIAA0344 against the NR database confirmed that these cDNA's are transcribed from the same genomic locus defined by two overlapping BACs (AC004765 and AC004803) from chromosome 12p13.3. Second, full sequence determination of a PCR fragment amplified from single-stranded cDNA confirmed the junction between the extended N34132 contig and KIAA0344\_h (AB002342). The 462 PCR product was amplified with primers CTCCTCAACAGACAGTGCAG (5' primer) and GACATTCTACTACTCGGTCTC (3' primer) designed from the N34132 extended contig and KIAA0344 sequences, respectively. The region of N34132 containing the start Met was isolated by PCR from a testis cDNA library (Clontech).

Human 5R69-17-2 (SEQ ID NO:67, SEQ ID NO:187)

The full-length ORF for 5R69-17-2 was isolated by screening a cDNA library using a probe derived from 5R69-17-2.

Human H85811 (SEQ ID NO:68, SEQ ID NO:188)

Tblastn, Smith-Waterman and blastn analyses using cDNA databases revealed an extension to encompass full-length ORF for H85811. The full ORF was reconstructed from Incyte ESTs 202971.8, 034583.3 and 034583.1 and public ESTs H85811 and AI570599.

Human R43524 (SEQ ID NO:73, SEQ ID NO:192)

Blastn analysis revealed an extension to encompass the complete catalytic region and the C-terminus of R43524. Since the initial filing of this application, the partial R43524 sequence appeared in the public database as the full-length gene encoding the heme-regulated initiation factor 2-alpha kinase (HRI) (AF181071).

Human AA088547 (SEQ ID NO:78, SEQ ID NO:197)



Genewise and Genescan analyses of genomic databases revealed an extension to encompass the complete ORF for AA088547.

Human orthologue of AA139478\_m (SEQ ID NO:80, SEQ ID NO:199)

Tblastn identified the Incyte 211475.1 as the potential full-length human  
5 orthologue of murine AA139478

Human AA232253 (SEQ ID NO:82, SEQ ID NO:201)

The full-length ORF for AA232253 was isolated by screening a cDNA library using a probe derived from AA232253. Since the initial filing of this application, the AA232253 sequence appeared in the public database as the full-length gene encoding SLK  
10 (AB011422). SLK is a stress-regulated mixed lineage kinase-like protein that activation of Rac and induction of apoptosis. cDNA library screening revealed multiple isoforms for this gene which are summarized in the Table below.

Table 9. Isoforms for AA232253

<b>Kestrl Name</b>	<b>Kestrl AA Acc #</b>	<b>Isoform type</b>	<b>Description*</b>
MLK4	AA232253	MLK4	Substitution of C for W at 346
		MLK4B	Different Cterm (332-800); seq in MLK4B is as shown in *

\* C-terminus specific to MLK4B

LPLAARMSEESYFESKTEESNSAEMSCQITATSN GEGHGMNPSLQAMMLMGFGDI  
FSMNKAGAVMHSGMQINMQAKQNSS

20 KTTSKRRGKKVNMALGFSDFDLSEGDDDDDDDDGEEEDNDMDNSE

Human H97685 (SEQ ID NO:84, SEQ ID NO:203)

Blastn analysis revealed an extension to encompass the full-length ORF for H97685. The full ORF was reconstructed from Incyte 474824.1 and the public ESTs  
25 H97685 and M62021.

Human AI052250 (SEQ ID NO:87, SEQ ID NO:206)

Blastn analysis revealed an extension to encompass the full-length ORF for AI052250. The full ORF was reconstructed from Incyte 396868.1, the public partial cDNA FLJ10074 (minus intron) and the public ESTs and the public ESTs AI052250 and H97685, AI499220 and M62021.

5 Human AA278842 (SEQ ID NO:88, SEQ ID NO:206)

A nearly full-length cDNA (FL4F12) for AA278842 was isolated by screening a cDNA library using a probe derived from AA278842. A full-length virtual ORF was generated using FL4F12 and AA278842.

Human AA599286 (SEQ ID NO:89, SEQ ID NO:208)

10 Since the initial filing of this application, the partial AA599286 sequence appeared in the public database as a full-length ORF (AK000342).

Human AA425725 (SEQ ID NO:90, SEQ ID NO:209)

Since the initial filing of this application, the partial AA425725 sequence appeared in the public database as MSSK1, a serine kinase gene located from human chromosome  
15 Xq28.

Human SGK022 orthologue of AA060026\_m (SEQ ID NO:91, SEQ ID NO:210)

Tblastn, Smith-Waterman and blastn analyses of cDNA and genomic databases  
databases revealed a potential human orthologue for murine AA060026. The full-length  
ORF for SGK022 was reconstructed from genomic locus AC022307.

20 Human AA399669 (SEQ ID NO:93, SEQ ID NO:212)

Blastn analysis revealed an extension to encompass the full-length ORF for AA399669. The full ORF was reconstructed as follows: sequence 1-1007 from AL136295.2; sequence 1008-2319 from AA399669 and Incyte 428177.1.

Human AA883975 (SEQ ID NO:95, SEQ ID NO:214)

25 Genescan and Genewise analyses of the genomic databases revealed an extension for AA883975 to encompass the full-length ORF

Human AA905446 (SEQ ID NO:96, SEQ ID NO:215)

Tblastn, Smith-Waterman and blastn analyses of cDNA and genomic databases  
databases revealed an extension for AA905446 to encompass the full-length ORF. For the  
30 Smith-Waterman analysis murine STK22 ( NP\_033462) was used as the closest  
orthologue. Contig formation: range 162133-163687 from HGP\_h 6921333\_9; removed  
intron (146-893) predicted from blastx analysis.

Human H29974 (SEQ ID NO: 97 SEQ ID NO:216)

Blastn analysis revealed an extension to encompass a complete catalytic ORF for AA399669. The nearly full-length ORF was reconstructed using Incyte 213829.1 and H29974.

5 Human AA215311 (SEQ ID NO:99, SEQ ID NO:218)

Blastn analysis revealed an extension to encompass the full-length ORF for AA21531. The full ORF was reconstructed from Incyte 067584.1, 022456.1, AA215311 and the reverse complement of CPG\_043208.

Human AA018361 (SEQ ID NO:100, SEQ ID NO:219)

10 The full-length ORF for AA018361 was isolated by screening a cDNA library using a probe derived from AA018361. This yielded clone Sug4-30. Clone Sug4-30, like multiple, independent cDNA clones contained a 181bp intron. The existence of intron-less RNA's was confirmed by a PCR reaction that generated a product that upon sequence analysis skipped the intron region. The full-length virtual ORF for AA018361 was  
15 generated through a contig between AL117482 (seq 1-367) and the sequence for clone Sug4-30.

Human orthologue of AA396601\_m (SEQ ID NO:106, SEQ ID NO:225)

tBlastn and Smith-Waterman analyses of genomic sequence revealed an extension to encompass the full catalytic region for the human orthologue of AA396601. The ORF  
20 was reconstructed from Incyte 018653.9 (7261449H1, 6891740J1) and genomic sequence CPG\_040010.

Human orthologue of AA671275\_m (SEQ ID NO:108, SEQ ID NO:227)

Since the initial filing of this application, a potential human orthologue for murine AA671275 appeared in the public database as the full-length ORF for vaccinia related  
25 kinase 3 (BAA90769).

Human H05721 (SEQ ID NO:111, SEQ ID NO:230)

Genescan and Genewise analyses of genomic sequence revealed an extension to encompass the full-length ORF for H05721.

Human AI086865 (SEQ ID NO:112, SEQ ID NO:231)

30 Genescan and Genewise analyses of genomic sequence revealed an extension to encompass the full-length ORF for AI086865. The full-length ORF was reconstructed from Celera 17000102901516, Incyte 243269.1 and public AL1377531.

Human AA836348 (SEQ ID NO:113, SEQ ID NO:232)

Genescan and Genewise analyses of genomic sequence revealed an extension to encompass the full-length ORF for AA836348.

Human R86668 (SEQ ID NO:14, SEQ ID NO:233)

5 The full-length ORF for R86668 was isolated by screening a cDNA library using a probe derived from R86668. Since the initial filing of this application, the R8668 sequence appeared in the public database as the full-length gene mitogen-activated protein kinase kinase kinase 6 (MAP3K6) (NM\_00467).

Human 2R41-9-4 (SEQ ID NO: 16, SEQ ID NO:235)

10 The full-length virtual ORF for 2R41-9-4 was generated using genomic sequence to provide the Nterminus for the partial ORF predicted from clone 2R41-9-4

Table 10. Sequences deleted from the provisional patent due to duplication with other genes in the patent

Prov. SEQ ID NO: (na)	Prov. SEQ ID NO: (aa)
160	196
213	214
215	216
122	126
119	123
148	184
4	20
7	23
205	206
14	30
15	31
35	56
42	63
51	72
44	65
77	91

78	92
79	93
80	94
157	193

## Results

Table 1 documents the results from the analysis of the nucleic acid sequence data. From left to right the data presented is as follows. "Gene name" refers to the EST or PCR  
 5 fragment that defined the novel kinase. "Species" refers to the organism the sequence was derived from. "ID#" refers to the nucleic acid and amino acid sequence ID number designation from this patent. "Kinase family" and "Kinase group" refers to the protein kinase classification defined by sequence homology and based on previously established phylogenetic analysis [Hardie, G. and Hanks S. The Protein Kinase Book, Academic Press  
 10 (1995) and Hunter T. and Plowman, G. Trends in Biochemical Sciences (1977) 22:18-22 and Plowman G.D. *et al.* (1999) Proc. Natl. Acad. Sci. 96:13603-13610)]. "ORF Start", "ORF End", "ORF Length" refer to the open reading frame range and length as calculated by standard nucleic acid translation programs such as MapDraw (DNASStar). "DNA  
 15 Repeats" refers to regions of low complexity sequence or repetitive elements such as Alu, LINE, SINE, and LTR sequences. The chromosomal location (CHR localization) for 37 of the 110 novel protein kinases is shown on Table 1 (NA, not available). The methods for determining chromosomal position are outlined below, in Example 2.

Table 2 documents the results from the analysis of the amino acid sequence data. From left to right the data presented is as follows. "Gene name" refers to the EST or PCR  
 20 fragment that defined the novel kinase. "Species" refers to the organism the sequence was derived from. "ID#" refers to the nucleic acid and amino acid sequence ID number designation from this patent. "Kinase family" and "Kinase group" refers to the protein kinase classification defined by sequence homology and based on previously established phylogenetic analysis [Hardie, G. and Hanks S. The Protein Kinase Book, Academic Press  
 25 (1995) and Hunter T. and Plowman, G. Trends in Biochemical Sciences (1977) 22:18-22 and Plowman G.D. *et al.* (1999) Proc. Natl. Acad. Sci. 96:13603-13610)]. "nraa Score", "ID match aa", "Identity", "Similar", "nraa Match Acc#", "Description" refer to the data obtained using a Smith-Waterman search of the amino acid sequence against the non-



redundant protein database (Matrix: Pam100; gap open/extension penalties 14/1). "Kinase Domain Start", "Kinase Domain End", "Profile Start" and "Profile End" refer to data obtained using a Hidden-Markov Model to define catalytic range boundaries. The profile has a length of 261 amino acids, corresponding to the complete protein kinase catalytic domain. Proteins in which the profile recognizes a full length catalytic domain have a "Profile Start" of 1 and a "Profile End" of 261. The boundaries of the catalytic domain within the overall protein are noted in the "Kinase Domain Start" and "Kinase Domain End" columns.

The following abbreviations were used for kinases:

ASK	Apoptosis signal-regulating kinase
CaMK	Ca <sup>2+</sup> /calmodulin-dependent protein kinase
CCRK	Cell cycle-related kinase
CDK	Cyclin-dependent kinase
CK	Casein kinase
DAPK	Death-associated protein kinase
DM	myotonic dystrophy kinase
Dyrk	dual-specificity-tyrosine phosphorylating-regulated kinase
GAK	Cyclin G-associated kinase
GRK	G-protein coupled receptor
GuC	Guanylate cyclase
HIPK	Homeodomain-interacting protein
IRAK	Interleukin-1 receptor-associated kin
MAPK	Mitogen activated protein kinase
MAST	Micotubule-associated STK
MLCK	Myosin-light chain kinase
MLK	Mixed lineage kinase
NIMA	NimA-related protein kinase
PKA	cAMP-dependent protein kinase
RSK	Ribosomal protein S6 kinase
RTK	Receptor tyrosine kinase

SGK	Serum and glucocorticoid-regulated kinase
STK	serine threonine kinase
ULK	UNC-51-like kinase

The following abbreviations were used for species

H	Human
M	Murine
R	Rat
FV	Fowlpox virus
MT	<i>M. thermoautotrophicum</i>
CE	<i>Caenorhabditis elegans</i>
DM	<i>Drosophila melanogaster</i>
OS	<i>Oryza sativa</i>
SP	<i>Schizosaccharomyces pombe</i>
TP	<i>Tetrahymena pyriformis</i>
PI	<i>Petunia inflata</i>
NC	<i>Neurospora crassa</i>
MSV	<i>Medicago sativa</i>
MSV	Moloney murine sarcoma virus
SA	<i>Squalus acanthias</i>
CS	<i>Cucumis sativus</i>
GM	<i>Glycine max</i>
LL	<i>Lilium longiflorum</i>
TV	<i>Trichomonas vaginalis</i>
MP	<i>Mycoplasma pneumoniae</i>
DD	<i>Dictyostelium discoideum</i>
SC	<i>Saccharomyces cerevisiae</i>
MT	<i>Methanobacterium thermoautotrophicum</i>

### Domain and Motif Identification

A Hidden Markov model (HMM) (Krogh, A., Brown, M., Mian, I. S., Sjolander, K., and Haussler, D. (1994). Hidden Markov models in computational biology: Applications to protein modeling. *J. Mol. Biol.*, 235:1501-1531) was used to identify, both catalytic and extracatalytic domains. Table 4 shows extra-catalytic domains that were identified using the HMM program. Other domains such as coiled-coil and pest motifs were identified as described next.

Potential coiled-coil domains were identified using the COILS program ([www.ch.embnet.org/software/COILS\\_form.html](http://www.ch.embnet.org/software/COILS_form.html)). The matrix used was MTIDK with windows of 14, 21, 28 amino acids. Only regions scoring 0.5 or higher were considered to have potential coiled-coil domain region.

Protein sequences containing potential pest motifs were identified using the program PESTfind ([www.at.embnet.org/embnet/tools/bio/PESTfind/](http://www.at.embnet.org/embnet/tools/bio/PESTfind/)). PEST regions in proteins are by definition sequences that tend to be rich in proline, glutamic or aspartic acid, arginine and histidine; they have been associated with increased protein turnover rates (Rogers S. *et al.* (1986) *Science* 234, 364-368. The algorithm defines PEST sequences as hydrophilic stretches of amino acids greater than or equal to 12 residues in length. Such regions contain at least one P, one E or D and one S or T. They are flanked by lysine (K), arginine (R) or histidine (H) residues, but positively charged residues are disallowed within the PEST sequence. PESTfind produces a score ranging from about -50 to +50. By definition, a score above zero denotes a possible PEST region; a value greater than +5 defines a high probability that there is a PEST domain.

### **Identification of potential coiled-coil domains and PEST domains in N34132**

Potential coiled-coil domains were identified in N34132 (SEQ ID NO:183) using the COILS program. Only regions scoring 0.5 or higher were considered to have potential coiled-coil domain region. The amino acid positions within N34231 scoring for potential coil-coil regions are shown below.

Table 11 coiled-coil domains predicted for N34132

Coiled-coil Region	Amino acid range	Length (aa)
1	124-147	24
2	437-451	15
3	495-526	32
4	1,723-1,749	27

Potential PEST domains were identified in N34132 using PESTfind, a value greater than +5 defines a high probability that there is a PEST domain. The amino acid positions within N34132 scoring for potential PEST regions are shown below.

Table 12 Potential Pest domains identified in N34132

PEST Region	Score	Amino acid range	Amino Acid Length
1	+ 4.91	54-95	42
2	+11.4	537-570	34
3	+31.08	1293-1304	12
4	+10.15	1543-1565	23
5	+ 6.17	1698-1732	35

## 10 EXAMPLE 2. Chromosomal Localization of Novel Mammalian Protein Kinases

### Materials and Methods

Several sources were used to find information about the chromosomal localization of each of the genes described in this patent. First, the accession number for the nucleic acid sequence was used to query the Unigene database. The site containing the Unigene search engine is: <http://www.ncbi.nlm.nih.gov/UniGene/Hs.Home.html>. Information on map position within the Unigene database is imported from several sources, including the Online Mendelian Inheritance in Man (OMIM, <http://www.ncbi.nlm.nih.gov/Omim/searchomim.html>), The Genome Database (<http://gdb.infobiogen.fr/gdb/simpleSearch.html>), and the Whitehead Institute human physical map ([http://carbon.wi.mit.edu:8000/cgi-bin/contig/sts\\_info?database=release](http://carbon.wi.mit.edu:8000/cgi-bin/contig/sts_info?database=release)). For example, searching Unigene with W56561, an EST for a MAK-like kinase, the

following information is retrieved: Chr.14, D14S65-qTEL. The location of this gene on an "ideogram" of the cytogenetic map of chromosome 14 is also provided, showing that W56561 maps to the bottom of chromosome 14, between 14q31 and 14qTel. If Unigene has not mapped the EST, then the nucleic acid for the gene of interest is used as a query against databases, such as dbsts and htgs (described at [http://www.ncbi.nlm.nih.gov/BLAST/blast\\_databases.html](http://www.ncbi.nlm.nih.gov/BLAST/blast_databases.html)) containing sequences that have been mapped already. The nucleic acid sequence is searched using BLAST-2 at NCBI (<http://www.ncbi.nlm.nih.gov/cgi-bin/BLAST/nph-newblast>) and is used to query either dbsts or htgs. In addition to the Whitehead and GDB sites mentioned above, Stanford University maintains a useful site for chromosomal mapping from STS data (<http://www-shgc.stanford.edu/RH/rhserverformnew.html>). Matches in htgs are often resolved immediately because the genomic region hit is annotated in the htgs entry. If an exact match match is found (defined roughly as 99% identity over a region of about 100 base pairs or longer, excluding any repetitive sequence), then the mapped position of the entry in the database is assigned to the original kinase query. Once a cytogenetic region has been identified by one of these approaches, disease association is established by searching OMIM (see above for URL) with the cytogenetic location. OMIM maintains a searchable catalog of cytogenetic map locations organized by disease. A thorough search of available literature for the cytogenetic region is also made using Medline (<http://www.ncbi.nlm.nih.gov/PubMed/medline.html>). References for association of the mapped sites with chromosomal abnormalities found in human cancer can be found in: Knuutila, *et al.*, Am J Pathol, 1998, 152:1107-1123.

### Results

The chromosomal location for 37 of the 110 novel protein kinases is shown on Table 1. Three of the novel protein kinases were mapped to regions associated with cancer amplicons, as shown on this table. The regions were also cross-checked with the Mendelian Inheritance in Man database, which tracks genetic information for many human diseases, including cancer. References for association of the mapped sites with chromosomal abnormalities found in human cancer can be found in: Knuutila, *et al.*, Am J Pathol, 1998, 152:1107-1123. Association of these mapped regions with other diseases is



documented in the Online Mendelian Inheritance in Man (OMIM)  
(<http://www.ncbi.nlm.nih.gov/htbin-post/Omim>).

### EXAMPLE 3: Generation of Specific Immunoreagents

#### 5 Materials and Methods

Peptide sequences to extra-catalytic regions of novel kinases are chosen which are not homologous to other known kinases based on a Smith Waterman homology search against the non-redundant protein database and predicted to be antigenic based on the DNASTar Protean program. These peptides are conjugated to KLH using Glutaraldehyde.

10 Rabbits are immunized with the KLH-peptide conjugates by four injections three weeks apart. The rabbits are bled ten and fourteen days following the third injection and bled out ten days after the fourth. The serum is checked against the peptide by ELISA.

Table 13. Peptides to be used as immunogens for raising antibodies

Clone Name	SEQ ID NO (aa)	Peptide Sequence	Amino Location
AA8256850	124	KSRDNSRDSSQSEND	339-353
		TEKLRKSQDLPREPLP	372-386
		RGWRPYDIHS	223-232
5R79-46-1	126	FEGPRRNKEVMYK	224-236
		KDDYNETVHKKTE	451-463
		GTHPKDRNVEKLQ	541-553
		EVSKYQEYTNELQET	643-657
AA256100	129	IDDTSNFDDFPESDI	405-419
		TEPDYKSKDWVFL	427-439
		EEKKLRRSQHARKET	61-75
AA210825	130	SNKDTLRKRHYWRLD	507-521
		RHTTRKSSTTLRE	488-500
		FQNNTTNRYEYKEIPL	528-542
		GKHRKTGRDVAVK	668-680
		FPTKQESQLRNE	687-698

AA316804	132	ESHVHQEPSKRIPS	239-252
		HTKRKSSTMVKEGW	409-422
		PSDLDVERDEEAVK	375-388
		SPGQGKDHKDLSTSI	543-557
R47805	143	EPVGRWDQDYDRAVL	44-58
		KPKGPGGKRGHKRLI	325-339
		PTDVAQLPSRVPRDA	219-233
AA234451	167	DPFDWEKTGNDGSLT	293-307
		HPRPQEKDVWEE	374-385
		RENTDEVFPDEQLSD	340-354
		RSEITQPDRDIPLVR	427-441
AA460132	180	LKSYSTSSKKARPVL	222-236
		KKLDEVRLRGRKRS	237-251
		ETEKTAQGLSNLAKT	131-145
N34132	183	SGRRRRPTKSKGSKS	1848-1862
		PGTAPSKPPLTKAPV	1474-1488
		VDSDTQPKAPGIDD	1365-1378
		AHSLDKTSHSSTTGL	1253-1267
5R69-17-2	187	GTTREKTDRVKST	178-190
		HSEAPELHGKIRSSN	138-152
		DETVTPPQFSIV	87-98
		QYDVKSEIYS	204-213
AA278842	206	TVDPEKSVRDQAFKA	515-529
		DSSTADRWDDEDWGS	637-651
		SVSEDPTQLEEVEKD	539-553
AA836348	232	NAPTKRPRSSTVTEA	323-337
		LDSEEDYYTPQKVDV	514-528
		GDKASYRQPKHVEKL	409-423

EXAMPLE 4. Expression analysis of Novel Mammalian Protein KinasesGENE EXPRESSION ANALYSIS

## Tissue Arrays

“cDNA libraries” derived from a variety of sources were immobilized onto nylon  
5 membranes and probed with <sup>32</sup>P-labeled cDNA fragments derived from the gene(s) of  
interest.

Total RNA or mRNA was used as template in a reverse transcription reaction to  
generate single-stranded cDNAs (ss cDNA) that were tagged with specific sequences at  
each end. An oligo dT primer containing a specific sequence (CDS:  
10 AAGCAGTGGTAACAACGCAGAGTACT30VN (V=A,G,C N=A,G,C,T)) anneals at  
the polyA track at the 3' end of the mRNA and the reverse transcriptase (MMLV  
RnaseH-) transcribes the antisense strand until it reaches the end of the RNA strand when  
it adds additional C residues. If a primer (SMII:

AAGCAGTGGTAACAACGCAGAGTACGCGGG or ML2G:

15 AAGTGGCAACAGAGATAACGCGTACGCGGG) ending with 3 Gs is added, it anneals  
to the added Cs and the MMLV recognizes the rest of the primer sequence as template and  
continues transcription. As a result, the synthesized cDNAs contain specific sequence tags  
at both the 5' and the 3' end. When the 5' and the 3' ends are tagged with the same  
sequence (CDS and SMII) it is referred to as “symmetric.” When the 5' end is tagged  
20 with a different sequence than the 3' end (CDS and ML2G) is referred to as “asymmetric”  
A double-stranded “cDNA library” is then generated by PCR amplification using the  
3'PCR and ML2 primers (3' PCR: AAGCAGTGGT<sup>6</sup>AACAACGCAGAGT and ML2:  
AAGTGGCAACAGAGATAACGCGT) that anneal to the added sequence tags.

The amplified “cDNA libraries” were manually arrayed onto nylon membranes  
25 with a 384 pin replicator. The DNA was denatured by alkali treatment, neutralized and  
cross-linked by UV light. The arrays were pre-hybridized with Express Hyb (Clontech)  
and hybridized with <sup>32</sup>P labeled probes generated by random hexamer priming of cDNA  
fragments corresponding to the genes of interest. After washing, the blots were exposed to  
phosphorimaging cassettes and the intensity of the signal was quantified. The amount of  
30 the DNA on the arrays was also quantified by treating non-denatured or denatured arrays  
with Syber Green I or Syber Green II respectively (1:100,000 in 50mM Tris, pH8.0) for 2  
minutes. After washing with 50mM Tris, pH8.0, the fluorescent emission was detected

with a phosphorimager (Molecular Dynamics) and quantified. The amount of the arrayed DNA was used to normalize the hybridization signal and the corrected values are tabulated in Table 3.

## 5 Results

The results of the microarray expression analysis of the protein kinases presented in this application is shown in Table 3. Data presentation from left to right is as follows: "Tissue": tissue type of the cDNA; "Tumor sym", indicates that the tissue is derived from a tumor, "sym" refers to the fact that the 5' and 3' primers used to make the sample are the same; "Normal Sym", indicates normal tissue was used to make the sample, with symmetric primers as described above; "Tumor 1o", indicates that primary tumor tissue was used to make the cDNA; "Tumor cells", indicates that these cDNA samples were made from cultured tumor cells; "Normal", indicates that these samples are derived from normal tissue or cell lines; "Endos", indicates that these samples are derived from endothelium-related tissue sources; "p53" refers to the status, mutant or wild-type, of the p53 gene in the source samples. Normalized expression values are presented for each gene referred to by its SEQ ID# on the subsequent columns. Genes represented in expression Table 3 are: SEQ ID NO:3 (AA826850), SEQ ID NO:5 (TBK1), SEQ ID NO:6 (AA305176), SEQ ID NO:8 (AA256100), SEQ ID NO:9 (CAB43292), SEQ ID NO:11 (EPK2), SEQ ID NO:12 (PKNbeta), SEQ ID NO:14 (H19102), SEQ ID NO:16 (RSK4), SEQ ID NO:17 (AAD30182), SEQ ID NO:20 (SGK2), SEQ ID NO:22 (PTK9L), SEQ ID NO:26 (AA383293), SEQ ID NO:29 (DRAK2), SEQ ID NO:31 (DRAK1), SEQ ID NO:032 (AA015726), SEQ ID NO:40 (MAK-V), SEQ ID NO:044 (TRAD), SEQ ID NO:044 (TRAD), SEQ ID NO:45 (AA454060), SEQ ID NO:47 (AA234451), SEQ ID NO:48 (AA436054), SEQ ID NO:49 (AA626859), SEQ ID NO:51 (KIAA0904), SEQ ID NO:52 (AA789239), SEQ ID NO:54 (CCRK), SEQ ID NO:55 (CLK4), SEQ ID NO:56 (AA557536), SEQ ID NO:57 (W56561), SEQ ID NO:60 (AA579641), SEQ ID NO:63 (NEK7), SEQ ID NO:66 (CAMKKB), SEQ ID NO:68 (HIPK2), SEQ ID NO:72 (R19609), SEQ ID NO:73 (HRI), SEQ ID NO:78 (AA088547), SEQ ID NO:79 (AA449542), SEQ ID NO:082a (MLK4), SEQ ID NO:82 (MLK4b), SEQ ID NO:84 (RIP4), SEQ ID NO:88 (AA278842), SEQ ID NO:89 (AA195964), SEQ ID NO:90 (MSSK1), SEQ ID NO:93 (TSK4), SEQ ID NO:94 (AI025291), SEQ ID NO:95

(AA948538), SEQ ID NO:96 (AA905446), SEQ ID NO:97 (H85389), SEQ ID NO:100 (AA018361), SEQ ID NO:101 (AA311714), SEQ ID NO:110 (AA452647), SEQ ID NO:111 (AA310219), SEQ ID NO:112 (AI086865), SEQ ID NO:114 (MEKK6), and SEQ ID NO:116 (SuRTK106).

5

EXAMPLE 5. Kinase assays for Erk, JNK1 and p38 MAP kinases

293T cells were transiently transfected with HA- p38 or co-transfected with Flag-tagged wt MLK4A, kinase-dead MLK4A, wild-type MLK4B or kinase-dead MLK4B using Lipofectamine 2000 (Lifetech). Cells were lysed 36 hr post-transfection. Cell lysates normalized to contain equivalent amounts of HA-p38 were immunoprecipitated with anti-HA antibody (Mab HA-11, Babco). Immunoprecipitates were split in two portions, one portion was Western-blotted with anti- HA antibody and the other with a phospho-specific p38 antibody (Promega) to detect activated levels of p38. Activation of Erk1 and Jnk1 was measured similarly. (This example applies to AA232253 (SEQ ID NO:82, SEQ ID NO:201).)

15

Results:

In transient assays wild-type MLK4A and MLK4B (but not kinase-inactive MLK4A(K45M) or MLK4B(K45M)) activate Erk, JNK1 and p38 MAP kinases.

20

EXAMPLE 6. RAC1 guanine-exchange factor assay

293T cells were transiently transfected with HA-Rac1 or co-transfected with Flag-tagged Duet C, Duet E, Dbl and HA-Tiam-1. Cells were lysed 36 hour post-transfection. Cell lysates normalized to contain equivalent amounts of Rac1 were affinity precipitated with immobilized GST-PBD (p21-binding domain of Pak3). Bound proteins were Western blotted and probed with anti-HA antibody to detect levels of activated Rac1. ((This example applies to R199772 (Trad/Duet)(SEQ ID NO:44, SEQ ID NO:164).)

25

Results:

Duet C and Duet E both act as guanine nucleotide exchange factors on Rac1.



### CONCLUSION

One skilled in the art would readily appreciate that the present invention is well adapted to carry out the objects and obtain the ends and advantages mentioned, as well as those inherent therein. The molecular complexes and the methods, procedures, treatments, molecules, specific compounds described herein are presently representative of preferred embodiments are exemplary and are not intended as limitations on the scope of the invention. Changes therein and other uses will occur to those skilled in the art which are encompassed within the spirit of the invention are defined by the scope of the claims.

It will be readily apparent to one skilled in the art that varying substitutions and modifications may be made to the invention disclosed herein without departing from the scope and spirit of the invention.

All patents and publications mentioned in the specification are indicative of the levels of those skilled in the art to which the invention pertains.

The invention illustratively described herein suitably may be practiced in the absence of any element or elements, limitation or limitations which is not specifically disclosed herein. Thus, for example, in each instance herein any of the terms "comprising", "consisting essentially of" and "consisting of" may be replaced with either of the other two terms. The terms and expressions which have been employed are used as terms of description and not of limitation, and there is no intention that in the use of such terms and expressions of excluding any equivalents of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the invention claimed.

In particular, although some formulations described herein have been identified by the excipients added to the formulations, the invention is meant to also cover the final formulation formed by the combination of these excipients. Specifically, the invention includes formulations in which one to all of the added excipients undergo a reaction during formulation and are no longer present in the final formulation, or are present in modified forms.

In addition, where features or aspects of the invention are described in terms of Markush groups, those skilled in the art will recognize that the invention is also thereby described in terms of any individual member or subgroup of members of the Markush

group. For example, if X is described as selected from the group consisting of bromine, chlorine, and iodine, claims for X being bromine and claims for X being bromine and chlorine are fully described.

Other embodiments are within the following claims.

What is claimed is:

CLAIMS

1. An isolated, enriched, or purified nucleic acid molecule encoding a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ  
5 ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ  
ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ  
ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ  
ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ  
ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ  
10 ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ  
ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ  
ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ  
ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ  
ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ  
15 ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ  
ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ  
ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ  
ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ  
ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ  
20 ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ  
ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ  
ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ  
ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ  
ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ  
25 ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ  
ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ  
ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ  
ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

2. The nucleic acid molecule of claim 1, wherein said nucleic acid molecule comprises a nucleotide sequence that:

(a) encodes a polypeptide comprising the amino acid sequence set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242;

(b) is the complement of the nucleotide sequence of (a);

(c) hybridizes under highly stringent conditions to the nucleotide molecule of (a) and encodes a naturally occurring kinase polypeptide;

(d) encodes a kinase polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it lacks one or more, but not all, of a domain selected from the group consisting of an N-terminal domain, a catalytic domain, a C-terminal domain, a coiled-coil structure region, a proline-rich region, a spacer region, an insert, and a C-terminal tail;

(e) is the complement of the nucleotide sequence of (d);



(f) encodes a domain of an amino acid sequence selected from the group set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, wherein said domain is selected from the group consisting of an N-terminal domain, a catalytic domain, a C-terminal domain, a coiled-coil structure region, a proline-rich region, a spacer region, an insert, and a C-terminal tail;

(g) is the complement of the nucleotide sequence of (f);

(h) encodes a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID

NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it lacks one or more, but not all, of the domains selected from the group consisting of an N-terminal domain, a catalytic domain, a C-terminal domain, a spacer region, a proline-rich region, a coiled-coil structure region, and a C-terminal tail; or

(i) is the complement of the nucleotide sequence of (h).

3. The nucleic acid molecule of claim 1, further comprising a vector or promoter effective to initiate transcription in a host cell.

4. The nucleic acid molecule of claim 1, wherein said nucleic acid molecule is isolated, enriched, or purified from a mammal.

5. The nucleic acid molecule of claim 4, wherein said mammal is a human.

6. A nucleic acid probe for the detection of nucleic acid encoding a kinase polypeptide in a sample, wherein said polypeptide is selected from the group consisting of  
5 SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141,  
10 SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166,  
15 SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196,  
20 SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241,  
25 and SEQ ID NO:242.  
30

7. The probe of claim 6, wherein said polypeptide is a fragment of the protein encoded by an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

8        A recombinant cell comprising a nucleic acid molecule encoding a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.



9. The cell of claim 8, wherein said polypeptide is a fragment of a protein encoded by an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

10. An isolated, enriched, or purified kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

11. The polypeptide of claim 10, wherein said polypeptide is a fragment of the protein encoded by an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

12. The polypeptide of claim 10, wherein said polypeptide comprises:

(a) an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ

ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242;

(b) an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ

ID NO:167, SEQ ID NO:168, SEQ ID NO 169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO 184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO 194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it lacks one or more, but not all of the domains selected from the group consisting of an N-terminal domain, a catalytic domain, a C-terminal domain, a spacer region, a proline-rich region, a coiled-coil structure region, and a C-terminal tail

(c) a domain of an amino acid sequence selected from the group set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID



NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 wherein said domain is selected from the group consisting of a C-terminal domain, a catalytic domain, an N-terminal domain, a spacer region, a proline-rich region, a coiled-coil structure region, and a C-terminal tail.

13. The kinase polypeptide of claim 10, wherein said polypeptide is isolated, purified, or enriched from a mammal.

14. The kinase polypeptide of claim 13, wherein said mammal is a human.

15. The kinase polypeptide of claim 10, wherein said polypeptide is a AA144574, AA116841, AA256100, AA305176, AA210825, AA316804, AA980090, N42050, AA476563, AA626690, AA960957, H19102, AA045601, AA107515, AA109508 or AA887783 polypeptide.

16. The kinase polypeptide of claim 10, wherein said polypeptide is a H60215, AA197883, AA297313, W30246, AA172300, AA383293, AA542015, H01248, N23936, W44160, 2R22-5-11, 5R72-18-1, AA021445, AA207220, AA426580, AA544838, W90839, 5R79-54-1, AA839940, R19772 or 5R72-8-2 polypeptide.

17. The kinase polypeptide of claim 10, wherein said polypeptide is a AA234451 polypeptide.

18. The kinase polypeptide of claim 10, wherein said polypeptide is a 5R65-16-1, AA061797, AA065538, AA124976, AA397553, AA435956, AA575635, AA626859, AA789239, AI086865, H17727, H29974, AA557536 or N28606 polypeptide.

19. The kinase polypeptide of claim 10, wherein said polypeptide is a AA631990 or W08549 polypeptide.

20. The kinase polypeptide of claim 10, wherein said polypeptide is a 5R72-16-2, R19927 or R43524 polypeptide.

21. The kinase polypeptide of claim 10, wherein said polypeptide is a 5R57-10-2 polypeptide.

5 22. The kinase polypeptide of claim 10, wherein said polypeptide is a AA232253 polypeptide.

23. The kinase polypeptide of claim 10, wherein said polypeptide is a AA430250, AA836348, R86668 or N34132 polypeptide.

10 24. The kinase polypeptide of claim 10, wherein said polypeptide is a AA098024 or SuRTK106 polypeptide.

25. The kinase polypeptide of claim 10, wherein said polypeptide is a R47805, AA099102, AA589241, H85811, AA013524, AA452647, AA840598, AA088547, AA139478, AA826850, R87679, W65887, H97685, W20810, AA599286, AA425725, AA103218, AA711829, AA060026, AA399669, AA758539, AA883975, AA948538, 15 AA018361, AA215311, AA311714, AA498104, 5R69-17-2, 5R69-23-3, 5R69-26-2, AA118352, AA396601, AA671275, AA278842, AA460132 or H05721 polypeptide.

26. An antibody or antibody fragment having specific binding affinity to a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

27. The antibody or antibody fragment of claim 26, wherein said polypeptide comprises:

(a) an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ

ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242;

(b) an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ

ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it lacks one or more, but not all, of the domains selected from the group consisting of a C-terminal domain, a catalytic domain, an N-terminal domain, a spacer region, a proline-rich region, a coiled-coil structure region, and a C-terminal tail.

(c) a domain of an amino acid sequence selected from the group set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID



NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID  
NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID  
NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID  
NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID  
5 NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID  
NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID  
NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID  
NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID  
NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID  
10 NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID  
NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID  
NO:241, and SEQ ID NO:242 wherein said domain is selected from the group consisting  
of a C-terminal domain, a catalytic domain, an N-terminal domain, a spacer region, a  
proline-rich region, a coiled-coil structure region, and a C-terminal tail.

28. A hybridoma which produces an antibody having specific binding affinity to a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

29. A method for identifying a substance that modulates kinase activity comprising:

(a) contacting a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136,

SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141,  
 SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146,  
 SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151,  
 SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156,  
 5 SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161,  
 SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166,  
 SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171,  
 SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176,  
 SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181,  
 10 SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186,  
 SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191,  
 SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196,  
 SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201,  
 SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206,  
 15 SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211,  
 SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216,  
 SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221,  
 SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226,  
 SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231,  
 20 SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236,  
 SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241,  
 and SEQ ID NO:242 with a test substance;

(b) measuring the activity of said polypeptide; and

(c) determining whether said substance modulates the activity of said

25 polypeptide.

30. A method for identifying a substance that modulates kinase activity in a cell comprising:

(a) expressing a kinase polypeptide in a cell, wherein said polypeptide is selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID  
 30 NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID

NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID  
NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID  
NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID  
NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID  
5 NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID  
NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID  
NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID  
NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID  
NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID  
10 NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID  
NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID  
NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID  
NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID  
NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID  
15 NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID  
NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID  
NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID  
NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID  
NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID  
20 NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID  
NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242;

- (b) adding a test substance to said cell; and
- (c) monitoring a change in cell phenotype or the interaction between  
said polypeptide and a natural binding partner.

31. A method for treating a disease or disorder by administering to a patient in need of such treatment a substance that modulates the activity of a kinase selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

32. The method of claim 31, wherein said disease or disorder is selected from the group consisting of immune-related diseases and disorders, cardiovascular disease, neurodegenerative disorders, and cancer.

33. The method of claim 31, wherein said substance modulates kinase activity *in vitro*.



34. The method of claim 33, wherein said substance is a kinase inhibitor.

35. A method for detection of a kinase polypeptide in a sample as a diagnostic tool for a disease or disorder, wherein said method comprises:

- (a) contacting said sample with a nucleic acid probe which hybridizes  
5 under hybridization assay conditions to a nucleic acid target region of a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139,  
10 SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164,  
15 SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189,  
20 SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214,  
25 SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239,  
30 SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, said probe comprising the nucleic acid sequence encoding said polypeptide, fragments thereof, or the complements of said sequences and fragments; and

(b) detecting the presence or amount of the probe:target region hybrid as an indication of said disease.

36. The method of claim 35, wherein said disease or disorder is selected from the group consisting of immune-related diseases and disorders, cardiovascular disease, neurodegenerative disorders, and cancer.

37. A method for detection of a kinase polypeptide in a sample as a diagnostic tool for a disease or disorder, wherein said method comprises:

(a) comparing a nucleic acid target region encoding said kinase polypeptide in a sample, wherein said kinase polypeptide is selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ

ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or one or more fragments thereof, with a control nucleic acid target region encoding said kinase polypeptide, or one or more fragments thereof; and

- (b) detecting differences in sequence or amount between said target  
5 region and said control target region, as an indication of said disease or disorder.

38. The method of claim 37, wherein said disease or disorder is selected from the group consisting of immune-related diseases and disorders, cardiovascular disease, neurodegenerative disorders, and cancer.

Table 1

Gene Name	SP	Prov	Seq	O	NA	Prov	Seq	ID	AA	SEQ ID # na	SEQ ID # aa	Family	Group	Length NA	Length AA	ORF Start	ORF end	ORF Length	DNA Repeats	CHR localization
AA114574 m BARK2 m	H	1	17	1	1	1	1	122	1	1	1	AGC	GRK	2087	680	1	2084	2084	1	22q11
AA114574 m BARK2 m	M	1	17	2	2	2	2	123	2	2	2	AGC	GRK	1368	378	1	1135	1134	1	NA
AA114574 m BARK2 m	H	140	176	3	3	3	3	124	3	3	3	AGC	Mo3C111_C8	1789	419	8	1264	1257	285-304	NA
AA114574 m BARK2 m	H	11	27	4	4	4	4	125	4	4	4	AGC	Mo3C111_C8	3224	414	65	1308	1242	1	4p16.1
AA114574 m BARK2 m	H	207	208	5	5	5	5	126	5	5	5	AGC	Mo3C111_C8	3013	729	91	2278	2187	1	NA
AA114574 m BARK2 m	H	42	1820	6	6	6	6	127	6	6	6	AGC	NDR	1421	329	53	1039	987	1	10p11.2
AA114574 m BARK2 m	M	42	1820	7	7	7	7	128	7	7	7	AGC	NDR	582	88	3	268	264	1	NA
AA114574 m BARK2 m	H	3	19	8	8	8	8	129	8	8	8	AGC	NDR	4083	404	66	1477	1382	1	12q11
AA114574 m BARK2 m	H	5	21	9	9	9	9	130	9	9	9	AGC	PKC	3263	978	117	3050	2034	1	10q13 q13.3
AA114574 m BARK2 m	H	203	204	10	10	10	10	131	10	10	10	AGC	PKC	315	106	1	315	315	1	NA
AA114574 m BARK2 m	H	6	22	11	11	11	11	132	11	11	11	AGC	PKC	2873	890	1	2870	2870	1	2p21
AA114574 m BARK2 m	H	6	24	12	12	12	12	133	12	12	12	AGC	PKC	2870	889	1	2867	2867	2221-2280	NA
AA114574 m BARK2 m	H	12	28	13	13	13	13	134	13	13	13	AGC	PKC	979	205	2	618	615	1	NA
AA114574 m BARK2 m	H	9	25	14	14	14	14	135	14	14	14	AGC	SGK	1155	384	1	1152	1152	598-638	CH4p17
AA114574 m BARK2 m	H	10	26	15	15	15	15	136	15	15	15	AGC	SGK	1410	469	1	1407	1407	1	12q12 q13.1
AA114574 m BARK2 m	H	227	228	16	16	16	16	137	16	16	16	AGC	SGK	2238	745	1	2235	2235	1	Xq21.1
AA114574 m BARK2 m	H	1	1	17	17	17	17	138	17	17	17	AGC	SGK	1850	549	1	1847	1847	787-788	14q24.3
AA114574 m BARK2 m	H	13	28	18	18	18	18	139	18	18	18	AGC	SGK	1298	431	1	1293	1293	856-883	8q21 q22
AA114574 m BARK2 m	H	18	32	19	19	19	19	140	19	19	19	AGC	SGK	2432	430	75	1304	1280	1804-1830	NA
AA114574 m BARK2 m	H	131	187	20	20	20	20	141	20	20	20	AGC	SGK	1346	244	2	733	732	1	NA
AA114574 m BARK2 m	H	33	54	21	21	21	21	142	21	21	21	AGC	SGK	2250	448	36	1373	1338	1	NA
AA114574 m BARK2 m	H	36	57	22	22	22	22	143	22	22	22	AGC	SGK	1050	349	1	1047	1047	1	3p14.3
AA114574 m BARK2 m	H	37	58	23	23	23	23	144	23	23	23	AGC	SGK	2310	440	420	1738	1320	1	1p31.1 p32.3
AA114574 m BARK2 m	H	38	59	24	24	24	24	145	24	24	24	AGC	SGK	3240	882	7	2082	2078	1	NA
AA114574 m BARK2 m	H	39	60	25	25	25	25	146	25	25	25	AGC	SGK	1248	287	1	801	801	1	NA
AA114574 m BARK2 m	H	40	61	26	26	26	26	147	26	26	26	AGC	SGK	2424	888	1	2058	2058	1	NA
AA114574 m BARK2 m	H	41	62	27	27	27	27	148	27	27	27	AGC	SGK	2421	888	1	2418	2418	436-458	NA
AA114574 m BARK2 m	H	42	63	28	28	28	28	149	28	28	28	AGC	SGK	1828	373	262	1380	1119	1	NA
AA114574 m BARK2 m	H	43	64	29	29	29	29	150	29	29	29	AGC	SGK	2871	372	171	1286	1118	1	2q31-2q24.3
AA114574 m BARK2 m	H	44	65	30	30	30	30	151	30	30	30	AGC	SGK	1245	414	1	1242	1242	1	NA
AA114574 m BARK2 m	H	45	66	31	31	31	31	152	31	31	31	AGC	SGK	4321	1311	148	4078	3933	1	7p11 q11
AA114574 m BARK2 m	H	46	67	32	32	32	32	153	32	32	32	AGC	SGK	2311	438	871	2178	1308	1	11q22.1 11q22.3
AA114574 m BARK2 m	H	47	68	33	33	33	33	154	33	33	33	AGC	SGK	2190	729	1	2187	2187	1	NA
AA114574 m BARK2 m	H	48	69	34	34	34	34	155	34	34	34	AGC	SGK	1584	520	1	1580	1580	1	NA
AA114574 m BARK2 m	H	49	70	35	35	35	35	156	35	35	35	AGC	SGK	4139	1330	77	4086	3990	1	2q34 q37
AA114574 m BARK2 m	H	50	71	36	36	36	36	157	36	36	36	AGC	SGK	1350	230	3	882	880	1	NA
AA114574 m BARK2 m	H	51	72	37	37	37	37	158	37	37	37	AGC	SGK	5183	928	155	2032	2032	1002-1022	NA
AA114574 m BARK2 m	H	52	73	38	38	38	38	159	38	38	38	AGC	SGK	2281	828	103	1989	1887	1	NA
AA114574 m BARK2 m	H	53	74	39	39	39	39	160	39	39	39	AGC	SGK	2145	714	1	2142	2142	1	NA
AA114574 m BARK2 m	H	54	75	40	40	40	40	161	40	40	40	AGC	SGK	2625	874	1	2622	2622	1	21q11
AA114574 m BARK2 m	H	55	76	41	41	41	41	162	41	41	41	AGC	SGK	7710	2288	1	8458	8358	1	NA
AA114574 m BARK2 m	H	56	77	42	42	42	42	163	42	42	42	AGC	SGK	1251	127	1	381	381	1	NA
AA114574 m BARK2 m	H	57	78	43	43	43	43	164	43	43	43	AGC	SGK	3884	1287	1	3881	3881	1	3q13.3 q21
AA114574 m BARK2 m	H	58	79	44	44	44	44	165	44	44	44	AGC	SGK	2586	514	406	1947	1542	1	11p15.1 11p15.2
AA114574 m BARK2 m	H	59	80	45	45	45	45	166	45	45	45	AGC	SGK	1820	508	97	1820	1524	1	NA
AA114574 m BARK2 m	H	60	81	46	46	46	46	167	46	46	46	AGC	SGK	2452	478	406	1838	1434	1	NA
AA114574 m BARK2 m	H	61	82	47	47	47	47	168	47	47	47	AGC	SGK	1077	268	1	788	788	1	NA
AA114574 m BARK2 m	H	62	83	48	48	48	48	169	48	48	48	AGC	SGK	811	247	2	742	741	1	NA
AA114574 m BARK2 m	H	63	84	49	49	49	49	170	49	49	49	AGC	SGK	2615	288	2	889	888	1	NA
AA114574 m BARK2 m	H	64	85	50	50	50	50	171	50	50	50	AGC	SGK	4473	1400	1	4470	4470	1218-1238	NA
AA114574 m BARK2 m	H	65	86	51	51	51	51	172	51	51	51	AGC	SGK	1868	534	6	1867	1862	1	NA
AA114574 m BARK2 m	H	66	87	52	52	52	52	173	52	52	52	AGC	SGK	1868	337	1	1011	1011	1	NA
AA114574 m BARK2 m	H	67	88	53	53	53	53	174	53	53	53	AGC	SGK	1380	211	1	833	833	163-191	NA
AA114574 m BARK2 m	H	68	89	54	54	54	54	175	54	54	54	AGC	SGK	2488	498	34	1520	1487	1	NA
AA114574 m BARK2 m	H	69	90	55	55	55	55	176	55	55	55	AGC	SGK	1831	545	30	1684	1635	1	NA
AA114574 m BARK2 m	H	70	91	56	56	56	56	177	56	56	56	AGC	SGK	1760	419	1	1757	1757	516-536	NA
AA114574 m BARK2 m	H	71	92	57	57	57	57	178	57	57	57	AGC	SGK	1859	632	1	1858	1858	1	14q32
AA114574 m BARK2 m	H	72	93	58	58	58	58	179	58	58	58	AGC	SGK	1776	413	1	1768	1768	1	NA
AA114574 m BARK2 m	H	73	94	59	59	59	59	180	59	59	59	AGC	SGK	1428	253	198	1228	1238	1	NA
AA114574 m BARK2 m	H	74	95	60	60	60	60	181	60	60	60	AGC	SGK	3304	462	1	1386	1386	1	20q12 A-q14.20q
AA114574 m BARK2 m	H	75	96	61	61	61	61	182	61	61	61	AGC	SGK	2328	281	2	844	843	1	NA
AA114574 m BARK2 m	H	76	97	62	62	62	62	183	62	62	62	AGC	SGK	7378	1852	42	5887	5888	1	12p13.31

Table 1 (cont'd)

SP	Gene Name	Prov	Sq	ID NA	Prov	Sq	ID AA	SEQ ID # n	SEQ ID # as	Family	Group	Length NA	Length AA	ORF Start	ORF_end	ORF Length	DNA Repeats	CHR localization
H	BCOHL h	M	148	104	M	148	104	184	184	Other	CAC2 ce	2164	538	113	1717	1608	246-287	NA
M	AA711028 m	M	149	105	M	149	105	185	185	Other	CAC2 ce	1568	378	1	1134	1134		NA
M	AA009102 h CARIKRB	M	152	106	M	152	106	186	186	Other	CARIKRB	1787	508	1	1784	1784	85-84	12p23-q14
H	SR69 17.2 h	M	156	107	M	156	107	187	187	Other	CTR1	3387	241	1850	2572	723	496-521	NA
H	H45811 h	M	134	108	M	134	108	188	188	Other	DYRK	3903	1171	183	3695	3513	1326-1348	CHP7
H	AA02181 h DYRK3	M	135	109	M	135	109	189	189	Other	DYRK	2141	553	253	1911	1659	x	NA
M	AA589241 m DYRK3 m	M	133	110	M	133	110	190	190	Other	DYRK	741	188	3	508	504	x	NA
M	SR72 10.2 h R10927 h	M	109	111	M	109	111	191	191	Other	EFK	5163	1849	20	4860	4947	x	NA
M	RA3524 h R1 h R19509	M	111	112	M	111	112	192	192	Other	EFK	1893	630	1	1890	1890	x	7p22-p22.3
M	1700057510457 h	M	135	113	M	135	113	193	193	Other	Endop	3055	253	219	877	759	2283-2365	NA
M	AA013524 m	M	135	114	M	135	114	194	194	Other	Endop	928	218	1	848	848	x	NA
M	17000139801107 h IRAMK	M	137	115	M	137	115	195	195	Other	IRAK	1791	598	1	1788	1788	x	NA
M	AA040598 m IRAMK m	M	137	116	M	137	116	196	196	Other	IRAK	2243	382	1	1175	1176	x	NA
M	AA086547 h	M	138	117	M	138	117	197	197	Other	IRE	2789	922	1	2786	2766	x	NA
M	HGP 6844486	M	139	118	M	139	118	198	198	Other	KYK2 do	1857	322	179	1144	986	x	NA
M	AA449542 m	M	139	119	M	139	119	199	199	Other	KYK2 do	1251	280	2	841	840	602-821	NA
M	SR37 10.2 m TESK2 m	M	115	120	M	115	120	200	200	Other	LMAK	140	41	2	124	123	x	NA
M	AA312253 h	M	117	121	M	117	121	201	201	Other	LMAK	2403	600	1	2400	2400	x	NA
M	AJ35137 h	M	200	122	M	200	122	202	202	Other	LMAK	2508	835	1	2505	2505	x	NA
M	H97665 h	M	143	123	M	143	123	203	203	Other	RP	2384	834	181	2062	1902	2219-2238	NA
M	W20810 m	M	144	124	M	144	124	204	204	Other	RP	1073	289	3	899	897	x	NA
M	AA1744236 h	M	211	125	M	211	125	205	205	Other	SCV1 sc	2087	688	1	2084	2084	x	NA
M	AA522250 h	M	225	126	M	225	126	206	206	Other	SCV1 sc	1739	505	174	1888	1515	x	NA
M	AA278842 h	M	104	127	M	104	127	207	207	Other	SCV1 sc	2868	808	105	2528	2424	1764-1783	11q12-q13 Amplicon
M	AA599286 h	M	145	128	M	145	128	208	208	Other	SLOB7	1949	840	1	1949	1949	x	NA
M	AA425125 h	M	146	129	M	146	129	209	209	Other	SROPK	1802	533	1	1590	1599	x	XQ26
M	SGK022 h	M	149	130	M	149	130	210	210	Other	SROPK	1038	288	184	987	804	x	NA
M	AA060206 m SGK022 m	M	150	131	M	150	131	211	211	Other	STK2A	1004	268	147	950	804	x	NA
M	AA399869 h	M	186	132	M	186	132	212	212	Other	STK2A	1537	292	372	1244	878	x	14p11-q11
M	AA758539 h	M	187	133	M	187	133	213	213	Other	STK2A	1322	358	101	1174	1074	x	NA
M	AA83975 h	M	153	134	M	153	134	214	214	Other	STK2A	822	273	1	819	819	x	NA
M	AA905446 h	M	223	135	M	223	135	215	215	Other	TSK	1066	216	365	1012	846	x	NA
M	H29974 h	M	86	136	M	86	136	216	216	Other	UNC	1838	333	2	1000	999	x	NA
M	AA408104 m H29974 m	M	155	137	M	155	137	217	217	Other	UNC	1490	412	1	1236	1238	x	NA
M	AA215311 h	M	154	138	M	154	138	218	218	Other	UNC	2011	341	199	1221	1023	x	NA
M	AA018391 h	M	192	139	M	192	139	219	219	Other	UNC	2759	481	113	1555	1443	x	15q23
M	AA311714 h	M	150	140	M	150	140	220	220	Other	UNC	1876	565	138	1833	1695	x	NA
M	SGK384 h	M	106	141	M	106	141	221	221	Other	Unique	117	39	1	117	117	x	NA
M	AA210451 m SGK384 m	M	197	142	M	197	142	222	222	Other	Unique	2721	349	272	1288	1047	2251-2286	NA
M	SGK071 2 h	M	181	143	M	181	143	223	223	Other	Unique	2115	704	1	2112	2112	57-76, 318-337	NA
M	AA118352 m SGK071 m	M	182	144	M	182	144	224	224	Other	Unique	1729	540	3	1622	1620	x	NA
M	O18953 9 h	M	182	145	M	182	145	225	225	Other	Unique	2481	540	1	1620	1620	240-259	NA
M	AA306001 m	M	183	146	M	183	146	226	226	Other	Unique	1886	385	3	1097	1095	x	NA
M	AA671275 h VRK3	M	190	147	M	190	147	227	227	Other	VRK	1425	474	1	1422	1422	x	18q13
M	S15175 m VRK3 m	M	190	148	M	190	148	228	228	Other	VRK	1009	234	3	704	702	937-957	NA
M	AA452647 h MPK3	M	190	149	M	190	149	229	229	Other	VRK	918	305	1	915	915	x	3cen-3p21
M	H05721 h	M	202	150	M	202	150	230	230	Other	VRK	2688	581	95	1837	1743	x	1p32.3-3.1 Amplicon
M	A1086865 h	M	120	151	M	120	151	231	231	Other	VRK	2463	690	7	2100	2094	x	NA
M	AA383348 h	M	121	152	M	121	152	232	232	Other	VRK	2511	838	1	2508	2508	x	NA
M	R86668 h MKK6	M	220	153	M	220	153	233	233	Other	VRK	3036	1011	1	3033	3033	x	1p32.3 p11.1
M	PAK6 h SR95 20-11	M	128	154	M	128	154	234	234	Other	VRK	2180	719	1	2157	2157	x	20p12
M	SURTK106 h 2R41-9.4 h	M	128	155	M	128	155	235	235	Other	VRK	2480	495	1	1485	1485	x	12p12.3
M	AA098024 m	M	128	156	M	128	156	236	236	Other	VRK	1783	183	1	549	549	x	NA
M	SGA2399a h	M	87	157	M	87	157	237	237	Other	VRK	1812	387	88	1188	1101	1382-1382	NA
M	H08950 h CORK	M	101	158	M	101	158	238	238	Other	VRK	1359	452	1	1356	1356	x	9q21.1-q21.3
M	H093120 h TESK2	M	121	159	M	121	159	239	239	Other	VRK	3016	555	1	2960	2960	x	NA



Table 2

Patent Seq ID# na	Patent Seq ID# aa	Family	Group	nraa Pscore	Length aa	ID match aa	% Identity	% Similar	nraa Match ACC#	Description	Kinase Domain(s) start	Kinase Domain(s) end	Profile start	Profile end
H	1	122	AGC	GRK	2.7E-314	688	887	100	CAB45657.1	BARK2 [Homo sapiens]	181	453	1	261
M	2	123	AGC	GRK	1.30E-180	378	371	98	NP_037029.1	Adrenergic receptor kinase, beta 2 (G-protein-linked receptor kin)	3	143	121	261
M	3	124	AGC	03C11.1 ce	5.80E-106	419	282	71	CAB76471.1	Serine/threonine protein kinase [Homo sapiens]	26	286	1	261
H	4	125	AGC	03C11.1 ce	1.40E-137	414	414	100	CAB76471.1	Serine/threonine protein kinase [Homo sapiens]	23	283	1	261
H	5	126	AGC	03C11.1 ce	0	729	729	100	[NP_037386.1	TANK-binding kinase 1 [Homo sapiens]	9	304	1	261
H	6	127	AGC	NDR	1.20E-09	329	73	48	BAA76817.1	KIAA0973 protein [Homo sapiens]	35	310	1	261
M	7	128	AGC	NDR	1.30E-19	88	42	49	AAF55594.1	CG7719 gene product [Drosophila melanogaster]	24	44	242	261
H	8	129	AGC	NDR	6.10E-181	484	463	100	BAA76809.1	KIAA0965 protein [Homo sapiens]	90	383	1	261
H	9	130	AGC	PKC	8.60E-160	978	615	67	NP_002133.1	Protein kinase C, $\mu$ [Homo sapiens]	651	907	1	261
H	10	131	AGC	PKC	1.10E-10	105	42	42	P05127	Protein kinase C, $\beta$ TA-II TYPE (PKC-BETA-2) [Homo sapiens]	19	24	256	261
H	11	132	AGC	PKC	0	890	890	100	NP_005804.1	Protein kinase C, $\nu$ [Homo sapiens]	578	832	1	261
H	12	133	AGC	PKC	9.4E-319	889	889	100	NP_037487.1	PKNbeta [Homo sapiens]	559	818	1	261
M	13	134	AGC	PKC	1.20E-108	205	204	100	JC7083	Protein kinase N beta [Homo sapiens]	1	134	126	261
H	14	135	AGC	S6K	3.60E-12	384	94	38	AAC2495.1	Ribosomal protein S6 kinase 3 [Homo sapiens]	81	333	1	261
H	15	136	AGC	S6K	2.90E-257	489	489	100	NP_036556.1	Ribosomal protein S6 kinase, 52kD, polypeptide 1 [Homo sapien	225	459	1	261
H	16	137	AGC	S8K	7.00E-176	745	745	100	NP_055311.1	Ribosomal protein S6 kinase, 80kD, polypeptide 8 [Homo sapien	73 & 426	330 & 683	1	261
H	17	138	AGC	S8K	9.60E-222	549	549	100	AAD30182.1	Unknown [Homo sapiens]	153	539	1	261
H	18	139	AGC	SGK	9.20E-103	431	430	100	AAD41091.1	SGK [Homo sapiens]	98	355	1	261
M	19	140	AGC	SGK	2.90E-157	430	426	99	NP_035491.1	Serum/glucocorticoid regulated kinase [Mus musculus]	98	354	1	261
M	20	141	AGC	SGK	2.00E-76	244	244	100	AAF12757.2	Protein kinase [Homo sapiens]	1	169	24	261
H	21	142	AGC	SGK	4.10E-211	446	375	88	AAF27051.1	SGK-like protein SGK [Homo sapiens]	182	369	1	261
H	22	143	Atypical	A6	5.60E-216	349	349	100	NP_009215.1	Protein tyrosine kinase 9-like (A8-related protein) [Homo sapiens]	10	17	253	261
H	23	144	CAMK	AMPK	1.40E-19	440	88	39	CAA04119.1	Phosphoprotein [Homo sapiens]	40	333	1	261
H	24	145	CAMK	CAMK	1.50E-185	699	468	85	O15075	DCAMK1 [DOUBLECORTIN-LIKE AND CAM KINASE-LIKE 1]	388	625	1	261
M	25	146	CAMK	CAMK	1.60E-82	297	199	67	AAF26675.1	CPG16 [Mus musculus]	59	297	1	261
H	26	147	CAMK	CAMK	2.80E-48	708	181	44	O15075	DCAMK1 [DOUBLECORTIN-LIKE AND CAM KINASE-LIKE 1]	415	673	1	261
M	28	148	CAMK	CAMK	2.60E-31	808	147	55	AAF26675.1	CPG16 [Mus musculus]	514	771	1	261
M	29	149	CAMK	DAPK	3.10E-121	372	372	100	NP_004217.1	Death-associated protein kinase-related 2	33	293	1	261
M	30	150	CAMK	DAPK	7.90E-93	372	340	91	NP_004217.1	Death-associated protein kinase-related 2	32	293	1	261
H	31	151	CAMK	DAPK	1.20E-113	414	414	100	NP_004751.1	Death-associated protein kinase-related 1	61	321	1	261
H	32	152	CAMK	EMK	5.90E-185	1311	1053	80	BAA76843.1	KIAA0999 protein [Homo sapiens]	8	259	1	261
H	33	153	CAMK	EMK	1.20E-45	436	153	51	T22427	Hypothetical protein F49C5.4 - [Caenorhabditis elegans]	74	325	1	261
H	34	154	CAMK	EMK	1.40E-32	438	122	48	AAC15093.1	Cdc25C associated protein kinase C-TAK1 [Homo sapiens]	56	307	1	261
M	35	155	CAMK	EMK	1.30E-184	729	729	100	AAC15093.1	Cdc25C associated protein kinase C-TAK1 [Homo sapiens]	59	340	1	261
M	36	156	CAMK	EMK	3.50E-126	462	462	100	AAC33487.1	R31237, 1, partial CDS [Homo sapiens]	999	1258	1	261
M	37	157	CAMK	EMK	0	1330	1235	100	BAA09484.1	KIAA0135 gene, related to p11-1 oncogene, [Homo sapiens]	1	158	23	261
M	38	158	CAMK	EMK	5.10E-59	230	183	79	BAA09484.1	KIAA0135 gene, related to p11-1 oncogene, [Homo sapiens]	20	271	1	261
H	39	159	CAMK	EMK	3.00E-111	928	638	100	BAA34501.1	KIAA0761 protein [Homo sapiens]	53	304	1	261
H	40	160	CAMK	EMK	7.30E-80	629	387	57	NP_055655.1	KIAA0537 gene product [Homo sapiens]	61	320	1	261
H	41	161	CAMK	EMK	1.40E-244	714	714	100	NP_055401.1	Hormonally upregulated neu tumor-associated kinase [Homo sa	570	825	1	261
H	42	162	CAMK	MLCK	6.20E-76	874	211	83	AAAT3168.1	Skeletal muscle myosin light chain kinase [Gallus gallus]	620 & 1086	873 & 1356	1	261
M	43	163	CAMK	Tro	0	2268	2227	100	BAA2535.1	KIAA1297 protein [Homo sapiens]	3	78	186	261
M	44	164	CAMK	Tro	7.80E-37	127	67	99	BAA2535.1	KIAA1297 protein [Homo sapiens]	985	1239	1	261
M	45	165	CAMK	Tro	0	1287	1284	100	NP_008995.1	STK with Dbl- and pleckstrin homology domains [Homo sapiens]	116	381	1	261
H	46	166	CAMK	Unque	5.00E-20	514	114	41	P25323	MLCK [Dictyostelium discoideum]	34	313	1	261
H	47	167	CKI	CKI	3.30E-89	508	181	53	AAF58340.1	CG11533 gene product [Drosophila melanogaster]	21	471	1	261
H	48	168	CMGC	CDK	8.60E-98	478	188	57	AAF58340.1	CG11533 gene product [Drosophila melanogaster]	1	218	23	261
H	49	169	CMGC	CDK	9.60E-39	266	138	62	NP_036527.1	PFTAIRE protein kinase 1 [Homo sapiens]	1	191	23	261
H	49	169	CMGC	CDK	7.10E-48	247	148	59	NP_004187.1	Cyclin-dependent kinase-like 1 (CDC2-related kinase) [Homo sa	1	191	23	261

Table 2 (cont'd)

M	50	170	CMGC	CDK	2.90E-84	296	193	65	78	NP_004187.1	Cyclin-dependent kinase-like 1 (CDC2-related kinase) [Homo sapiens]	1	240	24	261
H	51	171	CMGC	CDK	1.10E-284	1490	1490	100	100	AAF36401.1	CDC2-related protein kinase 7 [Homo sapiens]	21	1020	1	261
H	52	172	CMGC	CDK	9.20E-101	534	377	82	82	AAF36509.1	NKIAMRE [Homo sapiens]	4	365	1	261
M	53	173	CMGC	CDK	1.40E-128	337	225	82	96	AAF34671.1	NKIATRE alpha [Rattus norvegicus]	1	28	235	261
M	54	174	CMGC	CDK	3.00E-88	211	159	79	84	NP_038251.1	Cell cycle related kinase [Homo sapiens]	1	153	134	261
H	55	175	CMGC	CLK	1.50E-242	499	436	91	93	NP_031740.1	Cyclin-dependent kinase-like 1 (CDC2-related kinase) [Homo sapiens]	177	493	1	261
H	56	176	CMGC	RCK	9.10E-89	544	343	57	64	AAD12719.1	Extracellular signal-regulated kinase 7, ERK7 [Rattus norvegicus]	13	305	1	261
H	57	177	CMGC	RCK	2.30E-189	419	419	100	100	NP_055041.1	Renal tumor antigen [Homo sapiens]	4	285	1	261
H	58	178	CMGC	RCK	1.50E-180	632	632	100	100	AAF37278.1	Intestinal cell kinase [Homo sapiens]	4	284	1	261
M	59	179	CMGC	RCK	1.60E-79	413	198	60	77	P20689	MLCK [Rattus norvegicus]	109	364	1	261
H	60	180	Microbial PK	YGR262.sc	2.50E-45	253	102	46	67	AAF50799.1	CG10673 gene product [Drosophila melanogaster]	101	187	65	147
H	61	181	Other	C26C2.ce	2.30E-156	509	258	100	100	CAB70684.1	Hypothetical protein [Homo sapiens]	2	267	1	261
M	62	182	Other	C26C2.ce	1.80E-152	281	243	94	98	CAB70684.1	Hypothetical protein [Homo sapiens]	59	86	235	261
H	63	183	Other	C26C2.ce	8.70E-300	1952	1193	99	99	NP_055838.1	KIAA0344 gene product [Homo sapiens]	221	479	1	261
H	64	184	Other	C26C2.ce	1.10E-254	535	535	100	100	NP_037524.1	Nuclear receptor binding protein [Homo sapiens]	73	327	1	261
M	65	185	Other	C26C2.ce	2.50E-208	376	372	98	100	NP_037524.1	Nuclear receptor binding protein [Homo sapiens]	1	170	85	261
H	66	186	Other	CAMKK	3.80E-148	588	588	100	100	AAD31507.1	Ca2+/calmodulin-dependent protein kinase beta [Homo sapiens]	165	448	1	261
H	67	187	Other	CTR1	9.90E-24	287	87	33	52	JQ1743	Hypothetical 33.6K protein - rabita fibroma virus	24	285	1	261
H	68	188	Other	DYRK	0	1171	1137	97	99	AAD52568.1	Nuclear body associated kinase 1a [Mus musculus]	199	527	1	261
H	69	189	Other	DYRK	2.10E-280	553	553	100	100	NP_003573.1	Dual-specific tyrosine-(Y)-phosphorylation regulated kinase 3	174	487	1	261
M	70	190	Other	DYRK	2.30E-95	168	149	90	96	NP_003573.1	Dual-specific tyrosine-(Y)-phosphorylation regulated kinase 3	78	103	235	261
H	71	191	Other	EIFK	0	1649	1493	90	96	NP_038747.1	GCN2 eIF2alpha kinase [Mus musculus]	280 & 590	539 & 1001	1	261
H	73	192	Other	EIFK	1.50E-220	630	630	100	100	NP_055228.1	Heme-regulated initiation factor 2-alpha kinase [Homo sapiens]	187	583	1	261
H	74	193	Other	Endop	2.50E-45	253	102	46	67	AAF50799.1	CG10673 gene product [Drosophila melanogaster]	101	187	65	147
M	75	194	Other	Endop	3.70E-45	216	100	45	84	AAF50799.1	(AE003587) CG10673 gene product [Drosophila melanogaster]	116	150	116	147
H	76	195	Other	IRAK	0	596	596	100	100	NP_009130.1	Interleukin-1 receptor-associated kinase M [Homo sapiens]	165	443	1	261
M	77	196	Other	IRAK	1.20E-170	392	293	75	85	NP_009130.1	Interleukin-1 receptor-associated kinase M [Homo sapiens]	1	239	19	261
H	78	197	Other	IRE	1.5e-323	922	746	82	89	NP_036148.1	Ire1, inositol-requiring 1 gene [Mus musculus]	516	777	1	261
H	79	198	Other	KYK2.dd	8.70E-40	225	102	45	82	AAF48758.1	CG8173 gene product [Drosophila melanogaster]	32	318	1	261
M	80	199	Other	KYK2.dd	5.90E-32	280	109	32	50	AAF48758.1	CG8173 gene product [Drosophila melanogaster]	12	266	1	261
M	81	200	Other	LMK	2.80E-17	41	37	92	95	NP_009101.1	Testis-specific kinase 2 [Homo sapiens]	12	39	101	128
H	82	201	Other	MLK	2.50E-282	800	799	100	100	AAF63490.1	Mixed lineage kinase [Homo sapiens]	18	259	1	261
H	83	202	Other	MLK	8.60E-251	835	835	100	100	AAD28632.1	Pulative protein-tyrosine kinase [Homo sapiens]	463	723	1	261
H	84	203	Other	RIP	2.20E-158	634	365	100	100	BAA32317.1	KIAA0472 protein [Homo sapiens]	357	620	1	261
M	85	204	Other	RIP	5.30E-158	289	288	100	100	AAF03133.1	Receptor interacting protein 3 [Mus musculus]	7	27	181	202
H	86	205	Other	SCY1.sc	0	688	688	100	100	CAB55300.1	Hypothetical protein [Homo sapiens]	57	83	50	78
H	87	206	Other	SCY1.sc	1.70E-209	505	354	98	98	BAA92598.1	KIAA1360 protein [Homo sapiens]	32	327	1	261
H	88	207	Other	SCY1.sc	2.20E-157	808	396	45	61	AAF56933.1	CG1873 gene product [Drosophila melanogaster]	65	131	47	116
H	89	208	Other	SLOB?	7.40E-196	649	649	100	100	BAA91097.1	Unnamed protein product [Homo sapiens]	230	305	81	143
H	90	209	Other	SRPK	5.80E-252	533	533	100	100	NP_055185.1	Serine/threonine kinase 23 [Homo sapiens]	79	531	1	261
H	91	210	Other	STK22A	3.80E-53	268	122	48	70	NP_033461.1	Serine/threonine kinase 22A (spermogenesis associated) [Mus musculus]	10	265	1	261
M	92	211	Other	STK22A	2.70E-52	268	127	48	68	NP_033462.1	Serine/threonine kinase 22B (spermogenesis associated)	10	265	1	261
H	93	212	Other	STK22A	4.80E-18	292	112	45	84	NP_033461.1	Serine/threonine kinase 22A (spermogenesis associated)	25	280	1	261
H	94	213	Other	STK22A	5.10E-123	358	322	90	96	NP_033462.1	Serine/threonine kinase 22B (spermogenesis associated) [Mus musculus]	12	272	1	261
H	95	214	Other	TSK	2.10E-33	273	122	46	62	NP_033461.1	Serine/threonine kinase 22A (spermogenesis associated)	12	267	1	261
H	96	215	Other	TSK	2.50E-32	216	93	41	58	NP_033462.1	Serine/threonine kinase 22B (spermogenesis associated)	1	213	7	261
H	97	216	Other	UNC	0.000062	333	57	36	56	AAD32787.1	Pulative protein kinase [Arabidopsis thaliana]	1	329	1	261
M	98	217	Other	UNC	0.002492	412	53	37	52	BAA77341.1	UNC-51-like kinase (ULK) 2 [Mus musculus]	80	408	1	261
H	99	218	Other	UNC	0.001096	341	50	38	56	BAA77341.1	UNC-51-like kinase (ULK) 2 [Mus musculus]	8	340	1	261
H	100	219	Other	UNC	1.90E-68	480	247	100	100	T17265	Hypothetical protein DKFZp434C131.1 - human (fragment)	57	313	1	261
H	101	220	Other	UNC	1.60E-208	565	468	98	96	BAA91270.1	Unnamed protein product [Homo sapiens]	4	265	1	261
H	102	221	Other	Unque	6.70E-10	39	27	69	90	AAD00575.1	Serum-inducible kinase [Homo sapiens]	1	39	84	124

Table 2 (cont'd)

M	103	222	Other	Unique	0.000022	349	38	30	50	CAA18118.1	Serine/threonine protein kinase like protein [Arabidopsis thaliana]	80	159	1	88
H	104	223	Other	Unique	0.000126	704	54	30	45	BAA86578.1	KIAA1284 protein [Homo sapiens]	1	246	25	261
M	105	224	Other	Unique	0.007385	540	25	42	61	AAF47916.1	Tie gene product [Drosophila melanogaster]	9	104	168	261
H	106	225	Other	Unique	0.31334	540	52	30	42	P10162	SALIVARY PROLINE-RICH PROTEIN PO (ALLELE K) [Homo sapiens]	1	272	18	73
M	107	226	Other	Unique	0.022946	365	25	34	57	NP_006276.1	testis-specific kinase 1 [Homo sapiens]	68	96	42	71
H	108	227	Other	VRK	3.10E-263	474	474	100	100	BAA90769.1	Vaccinia related kinase 3 [Homo sapiens]	247	318	63	136
M	109	228	Other	VRK	1.20E-111	234	191	82	90	BAA90769.1	(AB031052) vaccinia related kinase 3 [Homo sapiens]	7	78	63	136
H	110	229	Other	YPL236.sc	7.40E-144	305	304	100	100	AAC28337.1	MPSK [Homo sapiens]	20	290	1	261
H	111	230	Other	YO09.ce	5.10E-49	581	135	43	63	AAF46188.1	CG4523 gene product [Drosophila melanogaster]	156	507	1	261
H	112	231	STE	NEK	3.30E-30	698	122	48	67	P51854	NEK1 (NIMA-RELATED PROTEIN KINASE 1) [Mus musculus]	4	251	1	261
H	113	232	STE	NEK	2.70E-119	836	357	86	88	AAD31839.1	(AC007055) unknown [Homo sapiens]	52	308	1	261
H	114	233	STE	STE11	1.10E-291	1011	1011	100	100	NP_004663.1	mitogen-activated protein kinase kinase kinase 8 [Homo sapiens]	376	629	6	261
H	115	234	STE	STE20-02	7.70E-177	719	719	100	100	BAA94184.1	(AB040812) protein kinase PAK5 [Homo sapiens]	449	700	1	261
H	116	235	TK	RTK-20	4.90E-24	495	77	38	58	AAA88465.1	(U40827) protein tyrosine kinase [Mus musculus]	187	453	1	261
M	117	236	TK	RTK-20	5.30E-18	183	53	39	57	NP_032036.1	fibroblast growth factor receptor 3 [Mus musculus]	8	143	123	261
H	118	237	AGC	SGK	6.30E-112	367	367	100	100	AAF12757.2	SGK2alpha protein kinase [Homo sapiens]	35	292	1	261
H	120	238	CMGC	CDK	2.80E-137	452	452	100	100	NP_036251.1	Cell cycle related kinase [Homo sapiens]	4	287	1	261
H	121	239	Other	LIMK	6.50E-233	555	555	100	100	NP_009101.1	Testis-specific kinase 2 [Homo sapiens]	62	293	5	261



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Table 3

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Table 3 (cont'd)

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Table 3 (contd)

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Table 3 (cont'd)

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Table 3 (cont'd)

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Case	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100
Case 1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100
Case 2	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100
Case 3	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100
Case 4	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100
Case 5	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79																					

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Table 3 (cont'd)[illegible]



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Location	1990-91	1991-92	1992-93	1993-94	1994-95	1995-96	1996-97	1997-98	1998-99	1999-00	2000-01	2001-02	2002-03	2003-04	2004-05	2005-06	2006-07	2007-08	2008-09	2009-10	2010-11	2011-12	2012-13	2013-14	2014-15	2015-16	2016-17	2017-18	2018-19	2019-20	2020-21	2021-22	2022-23	2023-24	2024-25	2025-26	2026-27	2027-28	2028-29	2029-30	2030-31	2031-32	2032-33	2033-34	2034-35	2035-36	2036-37	2037-38	2038-39	2039-40	2040-41	2041-42	2042-43	2043-44	2044-45	2045-46	2046-47	2047-48	2048-49	2049-50	2050-51	2051-52	2052-53	2053-54	2054-55	2055-56	2056-57	2057-58	2058-59	2059-60	2060-61	2061-62	2062-63	2063-64	2064-65	2065-66	2066-67	2067-68	2068-69	2069-70	2070-71	2071-72	2072-73	2073-74	2074-75	2075-76	2076-77	2077-78	2078-79	2079-80	2080-81	2081-82	2082-83	2083-84	2084-85	2085-86	2086-87	2087-88	2088-89	2089-90	2090-91	2091-92	2092-93	2093-94	2094-95	2095-96	2096-97	2097-98	2098-99	2099-00	2100-01	2101-02	2102-03	2103-04	2104-05	2105-06	2106-07	2107-08	2108-09	2109-10	2110-11	2111-12	2112-13	2113-14	2114-15	2115-16	2116-17	2117-18	2118-19	2119-20	2120-21	2121-22	2122-23	2123-24	2124-25	2125-26	2126-27	2127-28	2128-29	2129-30	2130-31	2131-32	2132-33	2133-34	2134-35	2135-36	2136-37	2137-38	2138-39	2139-40	2140-41	2141-42	2142-43	2143-44	2144-45	2145-46	2146-47	2147-48	2148-49	2149-50	2150-51	2151-52	2152-53	2153-54	2154-55	2155-56	2156-57	2157-58	2158-59	2159-60	2160-61	2161-62	2162-63	2163-64	2164-65	2165-66	2166-67	2167-68	2168-69	2169-70	2170-71	2171-72	2172-73	2173-74	2174-75	2175-76	2176-77	2177-78	2178-79	2179-80	2180-81	2181-82	2182-83	2183-84	2184-85	2185-86	2186-87	2187-88	2188-89	2189-90	2190-91	2191-92	2192-93	2193-94	2194-95	2195-96	2196-97	2197-98	2198-99	2199-00	2200-01	2201-02	2202-03	2203-04	2204-05	2205-06	2206-07	2207-08	2208-09	2209-10	2210-11	2211-12	2212-13	2213-14	2214-15	2215-16	2216-17	2217-18	2218-19	2219-20	2220-21	2221-22	2222-23	2223-24	2224-25	2225-26	2226-27	2227-28	2228-29	2229-30	2230-31	2231-32	2232-33	2233-34	2234-35	2235-36	2236-37	2237-38	2238-39	2239-40	2240-41	2241-42	2242-43	2243-44	2244-45	2245-46	2246-47	2247-48	2248-49	2249-50	2250-51	2251-52	2252-53	2253-54	2254-55	2255-56	2256-57	2257-58	2258-59	2259-60	2260-61	2261-62	2262-63	2263-64	2264-65	2265-66	2266-67	2267-68	2268-69	2269-70	2270-71	2271-72	2272-73	2273-74	2274-75	2275-76	2276-77	2277-78	2278-79	2279-80	2280-81	2281-82	2282-83	2283-84	2284-85	2285-86	2286-87	2287-88	2288-89	2289-90	2290-91	2291-92	2292-93	2293-94	2294-95	2295-96	2296-97	2297-98	2298-99	2299-00	2300-01	2301-02	2302-03	2303-04	2304-05	2305-06	2306-07	2307-08	2308-09	2309-10	2310-11	2311-12	2312-13	2313-14	2314-15	2315-16	2316-17	2317-18	2318-19	2319-20	2320-21	2321-22	2322-23	2323-24	2324-25	2325-26	2326-27	2327-28	2328-29	2329-30</
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[illegible]

Table 3 (cont'd)

[illegible]





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Table 3 (contd.)

Tissue	Tumor type	Tumor size	Tumor color	Heart rate	Stroke	p32	STC 116 S
Arterio gland - h							84
Cervical node - h							834
Coronary artery - h							822
Coronary artery - h							0
Coronary artery - h							2801
Coronary artery - h							231
Coronary artery - h							686
Coronary artery - h							2227
Coronary artery - h							2719
Coronary artery - h							1303
Coronary artery - h							717
Coronary artery - h							762
Coronary artery - h							637
Coronary artery - h							648
Coronary artery - h							410
Coronary artery - h							0
Coronary artery - h							164
Coronary artery - h							614
Coronary artery - h							282
Coronary artery - h							280
Coronary artery - h							61
Coronary artery - h							167
Coronary artery - h							486
Coronary artery - h							284
Coronary artery - h							88
Coronary artery - h							141
Coronary artery - h							232
Coronary artery - h							0
Coronary artery - h							168
Coronary artery - h							2128
Coronary artery - h							91
Coronary artery - h							188
Coronary artery - h							180
Coronary artery - h							0
Coronary artery - h							178
Coronary artery - h							71
Coronary artery - h							1036
Coronary artery - h							102
Coronary artery - h							145
Coronary artery - h							123
Coronary artery - h							637
Coronary artery - h							140
Coronary artery - h							0
Coronary artery - h							0
Coronary artery - h							0
Coronary artery - h							1282
Coronary artery - h							1237
Coronary artery - h							85
Coronary artery - h							0
Coronary artery - h							0
Coronary artery - h							138
Coronary artery - h							141
Coronary artery - h							70
Coronary artery - h							88
Coronary artery - h							288
Coronary artery - h							0
Coronary artery - h							148
Coronary artery - h							203
Coronary artery - h							173
Coronary artery - h							0
Coronary artery - h							88
Coronary artery - h							180
Coronary artery - h							0
Coronary artery - h							0
Coronary artery - h							307
Coronary artery - h							16
Coronary artery - h							80
Coronary artery - h							71
Coronary artery - h							111
Coronary artery - h							0
Coronary artery - h							0
Coronary artery - h							0
Coronary artery - h							247
Coronary artery - h							136
Coronary artery - h							0
Coronary artery - h							0
Coronary artery - h							88
Coronary artery - h							231
Coronary artery - h							222
Coronary artery - h							0
Coronary artery - h							256
Coronary artery - h							687
Coronary artery - h							82
Coronary artery - h							442
Coronary artery - h							80
Coronary artery - h							0
Coronary artery - h							0
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Coronary artery - h							0
Coronary artery - h							0
Coronary artery - h							0
Coronary artery - h							

Table 3 (cont'd)

[illegible]

Table 3 (cont.)

[illegible]

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Table 3 (cont'd)[illegible]



Table 4

Gene Name	SP ID# na	ID# aa	Family	Group	Length_AA	Extra-Catalytic Domains (Amino acid positions)
69117_h beta_adrenergic	H	1	AGC	GRK	688	Regulator of G protein signaling domain 54-175; PH domain 559-652
AA144574_m	M	2	AGC	GRK	378	PH domain 249-337
AA210825_h	H	9	AGC	PKC	978	Phorbol esters/diacylglycerol binding domain (C1 domain) 238-287; PH domain 497-577
AA316804_h	H	11	AGC	PKC	890	Phorbol esters/diacylglycerol binding domain (C1 domain) 155-204 and 272-321; PH domain 417-532
AA887783_h	H	21	AGC	SGK	446	PX domain 13-120
AA021445_h 3	H	32	CAMK	EMK	1311	Vitamin K-dependent carboxylation/gamma-carboxyglutamic (GLA) domain 1072-1113
AA31237_1_h AAC3348	H	34	CAMK	EMK	729	UBA domain 327-365
AA06786_5_h	H	36	CAMK	EMK	1330	PAS domain 133-186, 247-280, 354-386
AA36720_h	H	41	CAMK	MLCK	874	WD domain, G-beta repeat 674-711
AA088547_h	H	42	CAMK	Trio	2287	Immunoglobulin domain 1-62, 97-153, 221-277, 518-578, 1617-1678; Fibronectin type III domain 301-390, 1697-1779
AA232253_h	H	44	CAMK	Trio	1287	RhoGEF domain 235-405; Fibronectin type III domain 870-955; Immunoglobulin domain 786-851; PH domain 419-528
AA599286_h	H	76	Other	IRAK	596	Death domain 26-106
AA836348_h	H	78	Other	IRE	922	PQQ enzyme repeat 39-76
PAK6_h	H	82	Other	MLK	800	SAM domain (Sterile alpha motif) 337-408
	H	89	Other	SLOB	649	PX domain 16-122
	H	113	STE	NEK	836	Regulator of chromosome condensation (RCC1) 387-427, 427-480, 483-532, 598-650
	H	115	STE	STE20-02	719	P21-Rho-binding domain 11-69

## FIGURE 1A

SEQ ID NO: 122\_X69117\_H BARK2\_H  
MADLEAVLADVSYLMAMEKSKATPAARASKRIVLPEPSIRSVMQKYLAERNEITFDKIFN  
QKIGFLLFKDFCLNEINEAVPQVKFYEEIKEYEKLDNEEDRLCRSRQIYDAYIMKELLSC  
SHPFSKQAVEHVQSHLSKKQVTSTLFQPYIEEICESLRGDI FQKFMESDKFTRFCQWKNV  
ELNIHLTMNEFSVHRI IGRGGFGEVYGCRKADTGKMYAMKCLDKKRI KMKQGETLALNER  
IMLSLVSTGDCPFI VCMTYAFHTPDKLCFILDLMNGGDLHYHLSQHGVFSEKEMRFYATE  
I ILGLEHVHNR FVVYRDLKPANILLDEHGHARISDLGLACDFS KKKPHASVGTHGYMAPE  
VLQKGTAYDSSADWFS LGCMFLKLLRGHSPFRQHKTCDKHEIDRMTLT VNVELPDTFSPE  
LKS LLEGLLQ RDVSKRLGCHGGGSQEVKEHSFFKGVDWQH VYLQKYPPPLI PPRGEVNAA  
DAFDIGSFDEEDTKGIKLLDCDQELYKNFPLVISERWQQEV TETVYEAVNADTDKIEARK  
RAKNKQLGHEEDYALGKDCIMHGYMLKLG NPF LTQWQRRYFYLF PNRLEWRGEGESRQNL  
LTMEQILSVEETQIKDKKCILFRIKGGKQFVLQCESDPEFVQWKELNETFKEAQRLLRR  
APKFLNKPRSGTVELPKPSLCHRNSNGL

SEQ ID NO: 123\_AA144574\_M BARK2\_M  
CFVVYRDLKPANILLDEYGHVRISDLGLACDFS KKKPHASVGTHGYMAPEVLQKGT CYDS  
SADWFS LGCMFLKLLRGHSPFRQHKTCDKHEIDRMTLT VNVQLPDAFSPELRS LLEGLLQ  
RDVSQRLGCGGGGARELKEHIFFKGIDWQH VYL RKYPPPLI PPRGEVNAA DAFDIGSFDE  
EDTKGIKLLDCDQDLYKNFPLVISERWQQEVVETIYDAVNADTDKIEARKKAKNKQLGQE  
EDYAMGKDCIMHGYMLKLG NPF LTQWQRRYFYLF PNRLEWRGEGESRQSLLTMEQIMSVE  
ETQIKDRKCILLRIKGGKQFVLQCESDPEFAQWLKELTCTFNEAQRLLRRAPKFLNKPRA  
AILEFSKPPLCHRNSSGL

SEQ ID NO: 124\_AA826850\_H  
MGSSMSAATARRPVFDDKEDVNFDHFQILRAIGKGSFGKVCIVQKRDTEKMYAMKYM NKQ  
QCIERDEV RN VFRELEILQEIEHVFLVNLWYSFQDEEDMFMVVDLLLGGDLRYHLQQN VQ  
FSEDTVRLYICEMALALDYLRGQHI IHRDVKPDNILLDERGHAHLTDFNIATI IKDGERA  
TALAGTKPYMAPEIFXS FVNGGTGYSFEVDWWSVGVMAYELLRGWRPYDIHSSNAVESLV  
QLFSTVSVQYVPTWSKEMVALLRKLLTVNPEHRLSSLQDVQAAPALAGVLWDHLSEKRVE  
PGFVPNKGR LHCDPTFELEEMILES RPLHKKKKRLAKNKS RDNSRDSSQSENDYLQDCLD  
AIQQDFVIFNREKLKRSQDLPREPLPAPESRDAAEPVEDEAERSALPMCGPICPSAGSG

SEQ ID NO: 125\_AA960957\_H  
MGGNHS HKPPVFDENEEVNFDHFQILRAIGKGSFGKVCIVQKRDTKKMYAMKYM NKQKCI  
ERDEV RN VFRELQIMQGLEHPFLVNLWYSFQDEEDMFMVVDLLLGGDLRYHLQQNVHFTE  
GTVKLYICELALALEYLQRYHI IHRDIKPDNILLDEHGHVHITDFNIATVVKGAERASSM  
AGTKPYMAPEVFQVYMDRGP GYSYPVDWWSLGITAYELLRGWRPYEIH SVTPIDEILNMF  
KVERVHYSSTWCKGMVALLRKLLTKDPESRVSSLHDIQSVPYLADMNWD AVFKKALMPGF  
VPNKGR LNC DPTFELEEMILES KPLHKKKKRLAKNRSRDG TKDSCPLNGHLQHCLETVRE  
EFIIFNREKLRRQQGQGSQQLD TDSRGGGQAQSKLQDGCNNNLLTHTCTRGCSS

SEQ ID NO: 126\_TBK1\_H  
MQSTSNHLWLLSDILGQGATANVFRGRHKKTGDLFAIKVFNNISFLRPVDVQMREFEVLK  
KLNHNKIVKLFAIEEETTTRHKVLIMEFCPCGSLYTVLEEPSNAYGLPESEFLIVLRDVV  
GGMNHLRENGIVHRDIKPGNIMRVIGEDGQSVYKLTDFGAARELEDDEQFVSLYGTEEYL  
HPDMYERAVLRKDHQKKYGATVDLWSIGVTFYHAATGSLPFRPFEGPRRNKEVMYKIITG  
KPSGAISGVQKAENGPIDWSGDMPVSCSLSRGLQVLLTPVLANI LEADQEKCWGFDQFFA  
ETSDILHRMVIHVFSLQQMTAHKIYIHSYNTATIFHEL VYKQTKI ISSNQELIYEGRRLV  
LEPGRLAQHF PKTTEENPIFVVSREPLNTIGLIYEKISLPKVHPRYDL DGDASMAKAITG  
VVCYACRIASTLLLYQELMRKGIRWLI ELIKDDYNETVHKKTEVVITLDFCIRNIEKTVK

## FIGURE 1B

VYEKLMKINLEAAELGEISDIHTKLLRLSSSQGTIETSLQDIDSRLSPGGSLADAWAHQE  
GTHPKDRNVEKLQVLLNCMTEIYYQFKKDKAERRLAYNEEQIHKFDKQKLYYHATKAMTH  
FTDECVKKYEAFLNKSEEWIRKMLHLRKQLLSLTNQCFDIEEEVSKYQEQYTNELQETLPQ  
KMFTASSGIKHTMTPIYPSSNTLVEMTLGMKKLKEEMEGVVKELAENNHILERFGSLTMD  
GGLRNVDC

SEQ ID NO: 127\_AA305176\_H

MDPTAGSKKEPGGGAATEEGVNRIAVPKPPSIEEFSIVKPISRGAFGKVYLGQKGGKLYA  
VKVVKKADMINKNMTHQVQAERDALALSKSPFIVHLYYSLQSANNVYLVMEYLIGGDVKS  
LLHIYGYFDEEMAVKYISEVALALDYLHRHGI IHRDLKPDNMLISNEGHIKLTDFGLSKV  
TLNRDINMMDILTTPSMAKPRQDYSRTPGQVLSLISSLGFNTPIAEKNQDPANILSACLS  
ETSQLSQGLVCPMSVDQKDTTPYSSKLLKSCLETVASNPGMPVKCLTSNLLQSRKRLATS  
SASSQSHTFISSVESECHSSPKWEKDCQV

SEQ ID NO: 128\_AA116841\_M

TRPIPWPEGEEKLSDNAQSAMDMLLTIDDSKRAGMRELKQHPLFSEVDWENLQHQTMPFV  
PQPDDETDTSYFEARNNAQHLLTVSGFSL

SEQ ID NO: 129\_AA256100\_H

MAMTAGTTTTFPMSNHTRERVTVAKLTLENFYSNLILQHEERETRQKKLEVAMEEEGLAD  
EEKKLRRSQHARKETEFRLRKRTLGLDDFESLKVIGRGAFGEVRLVQKKDTGHIYAMKI  
LRKSDMLEKEQVAHIRAERDILVEADGAWVVKMFYSFQDKRNLYLIMEFLPGGDMMTLLM  
KKDTLTTEEETQFYISETVLDAIDAIHQLGFIHRDIKPDNLLDDAKGHVKLSDFGLCTGLKK  
AHRTEFYRNLTHNPPSDFSQNMNSKRKAETWKKNRRQLAYSTVGTDPDYIAPEVFMQTGY  
NKLCDWWSLGVIMYEMLIGYPPFCSETPQETYRKVMNWKETLVFPPEVPISEKAKDLILR  
FCIDSENRIENSGVEEIKGHPFFEGVDWEHIRERPAAPIEIKSIDDTSNFDDFPESDIL  
QPVPNTTEPDYKSKDWVFLNYTYKRFEGLTQRGSIPTYMKAGKL

SEQ ID NO: 130\_AA210825\_H

DSLLPTPALGTPLPWPVVGSLRTPLSLESTRSPTQRLLPSTPKDPAILRSPPPARSFLG  
SPLSHHLLTRSRGSRTQGPPGPPGGSRVGSRRAVPGLPPWPPPPHYAGLPGSPGPGSP  
PPGGLELQSPPLLPQIPAPGSGVSFHIQIGLTREFVLLPAASELAHVKQLACSIVDQKF  
PECGFYGLYDKILLFKHDPTSANLLQLVRSSGDIQEGDLVEVVLASATFEDFQIRPHAL  
TVHSYRAPAFCDHCGEMLFGLVRQGLKCDGCGLNHYHKRCAFSIPNNCSGARKRRLSSTSL  
ASGHSVRLGTSESLPCTAEELSRSTTELLPRRPPSSSSSSSSASSYTGRPIELDKMLLSKV  
KVPHTFLIHSYTRPTVCQACKKLLKGLFRQGLQCKDCKFNCHKRCATRVPNDCLGEALIN  
GDVPMEEATDFSEADKSALMDESEDGVI PGSHSENALHASEEEEEEGEGGKAQSSLGYIPL  
MRVVQSVRHTTRKSSTTLREGWVWHYSNKDTLRKRHYWRLDCKCITL FQNNTTNRYYKEI  
PLSEILTVEAQNFSLVPPGTNPHCFEIVTANATYFVGEMPGGTGGPSGQGAEAARGLX  
ETAIRQALMPVILQDAPSAPGHAPHRQASLSISVSNSQIQENVDIATVYQIFPDEVLGSG  
QFGVVYGGKHKRKTGRDVAVKVIDKLRFP TKQESQLRNEVAILQSLRHPGIVNLECMFETP  
EKVFVMEKLHGDMLEMILSSEKGR LPERLT KFLITQILVALRHLHFKNIVHCDLKPEN  
LLASADPFPPQVKLCDFGFARIIGEKSFRRSVVGTPAYLAPEVLLNQGYNRSLDMWSVGVI  
MYVSLSGTFPFNEDEDINDQIQNAAFMYPASPWSHISAGAILINNLLQVKMRKRYSDVK  
SLSHPWLQEQYQTWLDLRELEGKMGERYITHESDDARWEQFAAEHPLPGSGLPTDRDLGGA  
CPPQDHDMQGLAERISVL

SEQ ID NO: 131\_AA127299\_H

IQFIIVGAKDLLAMDSNGLSDPYIKITNLSQKTKVIKKTLTPTWNETFFVHFPEKTTLEI  
ECWDHDTFSDDFIGKASISLAEIPALAEVDMWIDMKTKKGEFAGK

## FIGURE 1C

SEQ ID NO: 132\_AA316804\_H

MSANNSPPSAQKSVLPTAIPAVLPAASPCSSPKTGLSARLSNGSFSAPSLTNSRGSVHTV  
SFLQIGLTRESVTIEAQELSLSAVKDLVCSIVYQKFPECGFFGMYDKILLFRHDMNSEN  
ILQLITSADEIHEGDLVEVVLSALATVEDFQIRPHTLYVHSYKAPTFCDYCGEMLWGLVR  
QGLKCEGCGLNHYHKRCAFKIPNNCSGVRKRRLSNVSLPGPGLSVPRFLQPEYVALPSEES  
HVHQEPSKRIPSWSGRPIWMEKMVMCRVKVPHTFAVHSYTRPTICQYCKRLLKGLFRQGM  
QCKDCKFNCHKRCASKVPRDCLGEVTFNGEPSSLGTDTDIPMDIDNNDINSDSSRGLDDT  
EESPSPEDKMFFLDPSDLDERDEEAVKTI SPSTSNNIPLMRVVQSIKHTKRKSSTMVKE  
GWMVHYTSRDNLKRHYWRLDSKCLTLFQNESGSKYYKEIPLSEILRISSPRDFTNISQG  
SNPHCFEII TDTMVYFVGENNGDSSHPVLAATGVGLDVAQSWEKAIRQALMPVTPQASV  
CTSPGQGDHDKDLSTSI SVSNCQIQENVDISTVYQIFADEVLGSGQFGIVYGGKHKRKTGR  
DVAIKVIDKMRFP TKQESQLRNEVAILQNLHHPGIVNLECMFETPERVFVMEKLGHDML  
EMILSSEKSRLPERITKFMVTQILVALRNLHFKNI VHCDLKPENVLLASAEPFPQVKLCD  
FGFARIIGEKSFRRSVVGTPAYLAPEVLR SKGYNRSLDMWSVGVI IYVSLSGTFPFNEDE  
DINDQIQNAAFMYPPNPWREISGEAIDLINNLLQVKMRKRYSDKSLSHPWLDYQDTWLD  
LREFETRIGERYITHESDDARWEIHAYTHNLVYPKHFIMAPNPDDMEEDP

SEQ ID NO: 133\_PKNBETA\_H

MEEGAPRQPGPSQWPPPEDEKEVIRRAIQKELKIKEGVENLRRVATDRRH LGHVQQLLRSS  
NRRLEQLHGELRELHARILLPGPGPGAEPVASGPRPWAEQLRARHLEALRRQLHVELKV  
KQGAENMTHTCASGTPKERKLLAAAQQMLRDSQLKVALLRMKISSLEASGSPEPGPELLA  
EELQHRLHVEAAVAEGA KNVVKLLSSRRTQDRKALAEAAQALQESSQKLDLLRLALEQLL  
EQLPPAHPLRSRVTRRELRAAVPGYPQPSGTPVKPTALTGT LQVRLLGCEQLLTAVPGRSP  
AAALASSPSEGWLRTKAKHQGRGELASEVLAVLKVDNRVVGQTGWGQVAEQSWDQTFVI  
PLERARELEIGVHWRDWRQLCGVAFLRLEDFLDNACHQLSLSLVPQGLLFAQVTFCDPVI  
ERRPRLQRQERIFSKRRGQDFLRRSQMNLGMAAWGRLVMNLLPPCSSPSTISPPKGCPR  
PTTLREASDPATPSNFLPKKTPLGEEMTPPPKPPRLYLPQEPTSEETPRTKRPHMEPRTR  
RGPSPPASPTRKPPRLQDFRCLAVLGRGHFGKVLLVQFKGTGKYAIAKALKKQEVLSRDE  
IESLYCEKRILEAVGCTGHPFLLSLLVCFQTSSHARFVTEFVPGGDLMMQIHEDVFPEPQ  
ARFYVACVVLGLQLHEKKIIYRDLKLDNLLLDAAQGLFKIADFGLCKEGIGFGDRTSTFC  
GTPEFLAPEVLTQEAYTQAVDWWALGVLLYEMLVGECPPFGDTEEEVFDCI VNMDAPYPG  
FLSVQGLEFIQKLLQKCPEKRLGAGEQDAEEIKVQPPFRTTNWQALLARTIQPPFVPTLC  
GPADLRYFEGEFTGLPPALTPPAPHSLLTARQQAAFRDFDFVSERFLEP

SEQ ID NO: 134\_AI021023\_M\_PKNBETA\_M

LKWDNLLLDAAQGLFKIADFGLCKEGIGFGDRTSTFCGTPEFLAPEVLTQEAYTRAVDWWG  
LGVLLYEMLVGECPPFGDTEEEVFDCI VNMDAPYPGFLSVQGLEFIQKLLQKCPEKRLGA  
GEQDAEEIKVQPPFRTTNWQALLARTIQPPFVPTLCGPADLRYFEGEFTGLPPALTPPAP  
HSLLTARQQAAFRDFDFVSERFLEP

SEQ ID NO: 135\_H19102\_H

GGNIRGPWARGWKS LWTGLGTIRSDLEELWELRGHHYHLHQESLKPA PVLVEKPLPEWPVP  
QFINLFLPEFPPIRPIRGQQQLKILGLVAKGSFGTVLKVL DCTQKAVFAVKVVPKVVLQR  
DTRVQCKEEVSIQRQINHPFVHSLGDSWQGRHLFIMCSYCSTDLYSLWSAVGCFPEASI  
RLFAAELVLVLCYLHDLGIMHRDVKMENILLDERGHLKLTDFGLSRHVPQGAQAYTICGT  
LQYMAPEVLSSGGPYNHAADWWSLGVLLFSLATGKFPVAAERD HVAMLASVTHSDSEIPAS  
LNQGLSLLLHELLCQNPLHRLRYLHHFQVHPFFRGVAFDPELLQKQPVNFVTETQATQPS  
SAETMPFDDFDCDLESFLLYPIFA



## FIGURE 1D

SEQ ID NO: 136\_AA476563\_H

MEFFRIDSKDSASELLGLDFGEKLYSLKSEPLKPFFTLPDGDSASRSFNTSESKVEFKAQ  
DTISRGSDDSVPVISFKDAAFDDVSGTDEGRPDLLVNLPGELESTREAAAMGPTKFTQTN  
IGIIENKLLLEAPDVLCLRLSTEQCQAHEEKGIEELSDPSGPKSYSITEKHYAQEDPRMLF  
VAAVDHSSSGDMSLLPSSDPKFQQLGVVESAVTANNTESLFRICSPLSGANEYIASTDT  
LKTEEVLLFTDQTDLLAKEEPTSLFQRDSETKGESGLVLEGDKIEHQIFEDLDKKLALAS  
RFYIPEGCIQRWAAEMVVALDALHREGIVCRDLNPNNILLNDRGHIQLTYFSRWSEVEDS  
CSDSAIERMYCAPEVGAITEETEACDWWSLGAVLFELLTGKTLVECHPAGINTHTTLNMP  
ECVSEEARSLIQQLLQFNPLERLGAGVAGVEDIKSHPPFTTPVDWAELMR

SEQ ID NO: 137\_AA626690\_H

MLPFAPQDEPWDREMEVFSGGGASSGEVNGLKMOVDEPMEEGEADSCHDEGVVKEIPITHH  
VKEGYEKADPAQFELLKVLGQGSFGKVFLVRKKTGPDAGQLYAMKVLKKASLKVRDRVRT  
KMERDILVEVNHPFIVKLHYAFQTEGKLYLILDFLRGGDVFTRLSKEVLFTEEDVKFYLA  
ELALALDHLHQLGIVYRDLKPENILLDEIGHIKLTDFGLSKESVDQEKKAYSFCGTVEYM  
APEVVNRRGHSQSADWWSYGVLMFEMLTGTLPFQGKDRNETMNMILKAKLGMPQFLSAEA  
QSLLRMLFKRNPANRLGSEGVEEIKRHLEFFANIDWDKLYKREVQPPFKPASGKPDDTFCF  
DPEFTAKTPKDSPGLPASANAHQLFKGFSFVATSIAEYKITPITSANVLPPIVQINGNAA  
QFGEVYELKEDIGVGSYSVCKRCIHATTNMEFAVKIIDKSKRDPSEEIEILMRYGQHPNI  
ITLKDVFDDGRYVYLVTDLMKGGEILLDRILKQKCFEREASDILYVISKTVDYLHCQGVV  
HRDLKPSNIIYMDSESASADSIRICDFGFAKQLRGENGILLTPCYTANFVAPEVLMQQGYD  
AACDIWSLGVLFYTMLAGYTPFANGPNDTPEEILLRIGNGKFSLSGGNWDNISDGAKDLL  
SHMLHMDPHQRYTAEQILKHSWITHRDQLPNDQPKRNDVSHVVKGAMVATYSALTHKTFQ  
PVLEPVAASSLAQRRSMKKRTSTGL

SEQ ID NO: 138\_AA215680\_H

MSLVACECLPSPGLEPEPCSRARSQAHVYLEQIRNRVALGVPMTKRDYLVDAATQIRLA  
LERDVSEDYEAFAFNHYQNGVDVLLRGIHVDPNKERREAVKLKITKYLRRAEEIFNCHLQR  
PLSSGASPSAGFSSLRLRPIRTLSSAVEQLRGCRVVGVIKVLVQDPATGGTFVVKSLP  
RCHMVSRRERLTIIIPHGVPMYTKLLRYFVSEDSIFLHLEHVQGGTLWSHLLSQAHSRHSGL  
SSGSTQERMKAQLNPHLNLTPARLPSGHAPGQDRIALEPPRTSPNLLLAGEAPSTRPQR  
EAEGEPTARTSTSGSSDLPAKPGGHLHLQARRAGQNSDAGPPRGLTWVPEGAGPVLGGCG  
RGMDQSCLSADGAGRGCGRATWSVREEQVKQWAAEMLVALEALHEQGVLCDLHPGNLLL  
DQAGHIRLTYFGQWSEVEPQCCGEAVDNLYSAPVGGISELTEACDWWWSFGSLLYELLTG  
MALSQSHPSGIIQAHTQLQLPEWLSRPAASLLTELLQFEPTRRRLGMGEGGVSKLKSHPPFS  
TIQWSKLVG

SEQ ID NO: 139\_SGK\_H

MTVKTEAAKGTLTYSRMGMVAIIIAFMKQRRMGLNDFIQKIANNSYACKHPEVQSILKI  
SQPQEPPELMNANPSPPPSPSQQINLGPSSNPHAKPSDFHFLKVIGKGSFGKVLLARHKA  
EVFYAVKVLQKKAILKKKEEKHIMSENVLLKNVKNHPFLVGLHFSFQTADKLYFVLDYIN  
GGELFYHLQRERCFLEPRARFYAAEIASALGYLHSLNIVYRDLKPENILLDSQGHIVLTD  
FGLCKENIEHNSTTSTFCGTPEYLAPEVLHKQPYDRTVDWWCLGAVLYEMLYGLPPFYSR  
NTAEMYDNILNKPLQLKPNITNSARHLLLEGLLQKDRTKRLGAKDDFMEIKSHVFFSLINW  
DDLINKKITPPFNPVSGPNELRHFDPEFTEEPVPNSIGKSPDSVLVTASVKEAAEAFLG  
FSYAPPTDSFL

SEQ ID NO: 140\_AA107515\_M

MTVKAEAAARSTLTYSRMGMVAIIIAFMKQRRMGLNDFIQKIASNTYACKHAEVQSILKM  
SHPQEPPELMNANPSPPPSPSQQINLGPSSNPHAKPSDFHFLKVIGKGSFGKVLLARHKA



## FIGURE 1E

EVFYAVKVLQKKAILKKKEEKHIMSEENVLLKNVKNHPFLVGLHFSFQTADKLYFVLDYIN  
GGELFYHLQRERCFLEPRARFYAAEIASALGYLHSLNIVYRDLKPENILLDSQGHIVLTD  
XFQLRRIEHNGTTSTFCGTPEYLAPEVLHKQPYDRTVDWWCLGAVLYEMLYGLPPFYSRN  
TAEMYDNILNKPLQLKPNITNSARHLLLEGLLQKDRTKRLGAKDDFMEIKSHIFFSLINWD  
DLINKKITPPFNPVNSGPSDLRHFDPEFTEEPVPSSIGRSPDSILVTASVKEAAEAFLGF  
SYAPPVDSFL

SEQ ID NO: 141\_AA109508\_M

HLQRERRFLEPRARFYAAEVASAI GYLHSLNIIYRDLKPENILLDCQGHVVLTD FGLCKE  
GVEPEDTTSTFCGTPEYLAPEVLRKEPYDRAVDWWCLGAVLYEMLHGLPPFYSDVSQMY  
ENILHQPLQIPGGRTVAACDLLQSLLHKDQRQRLGSKADFLEIKNHVFFSPINWDDLYHK  
RLTPPFNPVNTGPADLKHFDPEFTQEAVSKSIGCTPDTVASSSGASSAFLGFSYAPEDDD  
ILDC

SEQ ID NO: 142\_AA887783\_H

MQRDHTMDYKESCPVXIPSSDEHREKKKRFTVYKVLVSVGRSEWFVFRRYAEFDKLYNT  
LKKQFPAXALKIPAKRIFGDNFDPDFIKQRRAGLNEFIQNLVRYPELYNHPDVRAFLQMD  
SPKHQSDPSEDEDERSSQKLHSTSQNINLGPSGNPHAKPTDFDFLKVIGKGSFGKVLLAK  
RKLDGKFYAVKVLQKKIVLNRKEQKHIMAERNVLLKNVKNHPFLVGLHYSFQTTEKLYFVL  
DFVNGGEGHVVLTD FGLCKEGIAISDTTTCGTPEYLAPEVIRKQPYDNTVDWWCLGAV  
LYEMLYGLPPFYCRDVAEMYDNILHKPLSLRPGVSLTAWSI LELLEKDRQNRLGAKEDF  
LEIQNHPPFFESLSWADLVQKKIPPPFNPVAGPDDIRNFDTAFTETVPYSVCVSSDYSI  
VNASVLEADDAFVGFSYAPPSDDLFL

SEQ ID NO: 143\_R47805\_H

MAHQGTGIHATEELKEFFAKARAGSVRLIKVVIEDEQLVLGASQEPVGRWDQDYDRAVLPL  
LDAQQPCYLLYRLDSQNAQGFWEFLAWS PDNSPVRLKMLYAATRATVKKEFGGGHIKDE  
LFGTVKDDLSFAGYQKHLSSCAAPAPLTS AERELQQIRINEVKTEISVESKHQTLQGLAF  
PLQPEAQRALQQLKQKMVNYIQMKDLERETIELVHTEPTDVAQLPSRVPRDAARYHFFL  
YKHTHEGDPLESVVFIYSMPGYKCSIKERMLYSSCKSRL LDSVEQDFHLEIAKKIEIGDG  
AELTAEFLYDEVHPKQHAFAKQAFAPKPGGKRGHKRLIRGPGENGDDS

SEQ ID NO: 144\_H60215\_H

MSKLRMKRRASDRGAGETSARAKALGSGISGNNAKRAGPFILGPRLGN SPVPSIVQCLAR  
KDGTDDFYQLKILTLERGDQGI ESQEERQ GKMLLHTEYSLLSLLHTQDGVVHHHGLFQD  
RTCEIVEDTESSRMVKKMKKRICLVLDCLCAHDFS DKTADLINLQHYVIKEKRLSERETV  
VIFYDVVRVVEALHQKNIVHRDLKLGNMVLNKRTHRITITNFCLGKHLVSEGDLLKDQRG  
SPAYISPDVLSGRPYRGKPSDMWALGVVLF TMLYGQFPFYDSIPQELFRKIKAAEYTIPE  
DGRVSENTVCLIRKLLVLD PQORLAAADVLEALSAI IASWQSLSSLSG PLQVVPDIDDQM  
SNADSSQEAKVTEEC SQYEFENYMRQQLLLAE EKSSIHDTRSWVPKRQFGSAPPVRLGH  
DAQPMTSLDTAILAQRYLK

SEQ ID NO: 145\_SGK324\_H

MASTRSIELEHFEERDKRPRPGSRRGAPSSSGGSSSSSGPKGNGLIPSPAHS AHCSFYRTR  
TLQALSSEKKAKKARFYRNGDRYFKGLVFAISSDRFRSFDALLIELTRSLSDNVNLPQGV  
RTIYTIDGSRKVTS LDELLEGESYVCASNEPFRKVDYTKNINPNWSVNIKGGTSRALAAA  
SSVKSEVKESKDFIKPKLVTVIRSGVKPRKAVRILLNKKTAHSFEQVLTDITEAIKXASG  
VVKRLCTLDGKQVRVTCVHLPDFFGDDDVFIACGPEKFRYAQDDFVLDHSECRVLKSSYS  
RSSAVKYSKSPGPSRRSQISAHGRSSSNVNGGP ELDRCSPEGVNGNRCSESSTLLEK  
YKIGKVI GDGNFAVVKECIDRSTGKEFALKIIDKAKCCGKEHLIENEVSILRRVKHPNII

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## FIGURE 1F

MLVEEMETATELFLVMELVKGGDLFDAITSSTKYTERDGSAMVYNLANALRYLHGLSIVH  
RDIKPENLLVCEYPDGTKSLKLGD FGLATVVEGPLYTVCGTPTYVAPXIIAETGYGLKVD  
IWAAGVITYILLCGFPPFRSENNLQEDLFDQILAGKLEFPAPYWDNITDSAKELISQMLQ  
VNVEARCTAGQILSHPWVSDDASQENNMQAEVTGKCLKQHFNALPKQNSTTTGVSVMVS  
GRRQVWPDCGAGLEVFEFGSRELPSHGSWCLP

SEQ ID NO: 146\_W30246\_M SGK324\_M  
TKSSSSSPTSPGSFRGLKISAQGRSSSNVNGGPELDRCLSPGCVNGNRCSESFPLLEKYR  
IGKVIGDGNFAVVKECVDRTYGKEFALKIIDKAKCCGKEHLIENEVSILRRVKHPNII ML  
VEEMETATDLFLVMELVKGGDLFDAITSSTKYTERDGSAMVYNLANALRYLHSLSIVHRD  
IKPENLLVCEYPDGTKSLKLGD FGLATVVEGPLYTVCGTPTYVAPEIIAETGYGLKVDVW  
AAGVITYILLCGFPPFRSENNLQEDLFDQILAGKLEFPAPYWDNITDSPCVCFRKCL

SEQ ID NO: 147\_AA383293\_H  
PAAKRVVYRNGDPFFPGSQLVVTQRRFPTMEAFLEVTSAVQAPLAVRALYTPCHGHPV  
TNLADLKNRGQYVAAGFERFHKLPYQAFCLSVFRNGDLVSPFSLKLSQAASQDWETVL  
KLLTEKVKLQSGAVRLCTLEGLPLSAGKELVTGHYYVAVGEDEFKDLPPALSTRGLLAA  
GNEAHLRSGVGTVAGSPKPLGRKAKKETCLIVTLTKYQQSETSRDGQSFPSPGVIGVYGA  
PHRRKETAGALEVADDEDTQTEEPLDQRAAQIVEQVTCLQDFFGDDDVFIACGPEKFRYA  
QDDFVLDHSRRRLREHQAGFEKLRRTRGEEKEAEKEKKPCMSGGRRMTLRDDQPAKLEK  
EPKTRPEENKPERPSGRKPRPMGI IANVEKHYETGRVIGDGNFAVVKECRHRETRQAYA  
MKIIDKSRLKGKEDMVDSEILIIQSLSHPNIVKLHEVYETDMEIYLILEYVQGGDLFDAI  
IESVKFPEPDAALMIMDLCKALVHMHDKSIVHRDLKPENLLVQRNEDKSTTLKLADFGLA  
KHVVRPIFTVCGTPTYVAPEILSEKGYGLEVDMWAAGVILYILLCGFPPFRSPXXGDQDE  
LFNIIQLGHFEFLPPYWDNISDAAKDLVSRLLVDPKKRYTAHQVLQHPWIETAGKTNTV  
KRQKQVSPSSDGHFRSQHKRVVEQVS

SEQ ID NO: 148\_AA197883\_M  
MPTAPVLRPPPPATPAPPAPSRPAPPPIPGHRGPCDHSLKCLSSKISERKLPGPWLPAGR  
GPLEKPVLGPRGAVMPLFSPQSSLHSVRAEHSPLKPRVVTVVKLGGQPLRKATLLLNRRS  
VQTFEQLLSDISEALGFPRWKNDVRKLFITLKGREVKSVSDFFREGDAFIAMGKEPLTLK  
SIQLAMEELYPKNRALALAPHSRVPSRLRSRLPSKLLKGS HRCEAGSYSAEMESKAVS  
RHQGKTSTVLAPEDKARAQKWVRGKQSESEPGGPPSPGAATQEETHASGEKHLGVEIEKTS  
GEIVRCEKCKRERELQLGLQREPCPLGTSELDLGRAQKR DSEKLVRTKSCRRPSKAKFTD  
GEEGWKGDSHRGSPRDPPQEMRRPNSNSDKKEIRGSESQDSYPQGA PKAQKDFVEGPPAV  
EEGPIDMRREDRHTCRSKHAAWLRREQQAEPQLPRTRGEEKQAEHEKKPGGLGERRAPE  
KESKRKLEEKRPERPSGRKPRPKGII SADVEKHYDIGGVIGDGNFATVKECRHRETKQAY  
AMKMIDKSQKKGKEDIVDSEILIIQSLSHPNIVKLHEVYETEAEIYLIMEYVQGGDLFDA  
IVENVKFPEPEAAVMITDLCKAFVHMHDKNIVHRDVKPENLLVQRNEDKSITLKLADFG  
AKYVVRPIFTVCGTPTYVAPEILSEKGYGLEVDMWAAGVILYILLCGFPPFRSPERDQDE  
LFNIIQVGQFEFLSPYWDNISDAAKDLVRNLLEVDPKKRYTAEQVLQHPWIEMVGHNTG  
NSQKEESPNSLGHFQSQHKKVAEQMP

SEQ ID NO: 149\_DRAK2\_H  
MSRRRFDCRSISGLLTTPQIPKMFNFNFYILTSKELGRGKFAVVRQCISKSTGQEYA  
AKFLKKRRRGQDCRAEILHEIAVLELAKSCPRVINLHEVYENTSEIILILEYAAGGEIFS  
LCLPELAEMVSENDVIRLIKQILEGVYYLHQNNIVHLDLKPQNILLSSIYPLGDIKIVDF  
GMSRKIGHACELREIMGTPEYLAPEILNYDPITTATDMWNIGIIAYMLLTHTSPFVGEDN  
QETYLNISQVNV DYSEETFSSVSQ LATDFIQSLLVKNPEKRPTAEICLSH SWLQQWDFEN

## FIGURE 1G

LFHPEETSSSSQTQDHSVRSSSEDKTSKSSCNGTCGDREDKENI PEDSSMVSKRFRFDDSL  
PNPHELVSDDLCC

SEQ ID NO: 150\_W44160\_M DRAK2\_M  
MSRRRFDCRSVSGLLTTTPQTPIKTENFNNFYTLTPKELGRGKFAVVRQCISKSTGQEYA  
AKSLKKRRRGQDCRAEILHEIAVLELARSCPHVINLHEVYENATEIILVLEYAAGGEIFN  
LCLPELAEMVSENDVIRLIKQILEGVHYLHQNNIVHLDLKPQNILLSSIYPLGDIKIVDF  
GMSRKIGNASELREIMGTPEYLAPEILNYDPITTATDMWNIGIIAYMLLTHTSPFVGEDN  
QETYNISQVNVVDYSEEMFSSVSQLATDFIQSLLVKNPEKRPTAESCLSHSWLQQWDFGS  
LFHPEETSGSSQIQDLTLRSSEEKTSKSSCNGSCGAREDKENI PEDGSLVSKRFRFDDSL  
PSPHELVPDLFC

SEQ ID NO: 151\_H01248\_H, DRAK1\_H  
MIPLEKPGSGGSSPGATSGSGRAGRGLSGPCRPPPPQARGLLTEIRAVVRTEPFQDGYS  
LCPGRELGRGKFAVVRKCIKKDSGKEFAAKFMRKRRKGQDCRMEI IHEIAVLELAQDNPW  
VINLHEVYETASEMILVLEYAAGGEIFDQCVADREEAFKEKDVQRLMRQILEGVHFLHTR  
DVVHLDLKPQNILLTSESPLGDIKIVDFGLSRILKNSEELREIMGTPEYVAPEILSYDPI  
SMATDMWSIGVLTIVMLTGISPFLGNDKQETFLNISQMNLSEYSEEEFDVLSESAVDFIRT  
LLVKKPEDRATAEECLKHPWLTQSSIQEPSFRMEKALEEANALQEGHSVPEINSDTDKSE  
TEESIVTEELIVVTSYTLGQCRQSEKEKMEQKAISKRFKFEEPLLQEIPGEFIY

SEQ ID NO: 152\_AA021445\_H  
MPARIGYYEIDRTIGKGNFAVVKRATHLVTKAKVAIKIIDKTQLDEENLKKIFREVQIMK  
MLCHPHIIRLYQVMETERMIYLVTEYASGGEIFDHLVAHGRMAEKEARRKFKQIVTAVYF  
CHCRNIVHRDLKAENLLLDANLNIAIDFGFSNLFTPGQLLKTWCGSPPYAAPELFEGKE  
YDGPKVDIWSLGVVLYVLVCGALPFDGSTLQNLRARVLSGKFRI PFFMSTECEHLIRHML  
VLDPNKRLSMEQICKHKWMLGDADPNFDRLIAECQQLKEERQVDPLNEDVLLAMEDMGL  
DKEQTLQSLRSDAYDHYSIYSLLCDRHKRHKTLLRLGALPSMPRALAFQAPVNIQAEQAG  
TAMNISVPQVQLINPENQIVEPDGTLNLDSDGEDEEPSPEALVRYLSMRRHTVGVADPRTE  
VMEDLQKLLPGFPGVNPQAPFLQVAPNVNFMHNLLPMQNLQPTGQLEYKEQSLLQPPTLQ  
LLNGMGPLGRRASDGGANIQLHAQQLLKRPRGPSPLVTMTPAVPAVTPVDEESSDGEPDQ  
EAVQRYLANRSKRHTLAMTNPTAEIPDLQRLQGLQPPFRSRVWPPHLVPDQHRSTYKDSN  
TLHLPTERFSPVRRFSDGAASIQAFKAHLEKMGNNSSIKQLQQECEQLQKMYGGQIDERT  
LEKTQQQHMLYQQEQHHQILQQQIQDSICPPQPSPLQAACENQPALLTHQLQRLRIQPS  
SPPPNHPNNHLFRQPSNSPPPMSSAMIQPHGAASSSQFQGLPSRSAIFQQQPENCSSPPN  
VALTCLGMQQPAQSQQVTIQVQEPVDMLSNMPGTAAGSSGRGISISPSAGQMOMQHRTNL  
MATLSYGHRPLSKQLSADSAEAHSLNVNRFSPANYPDQAHLPPLFSDQSRGSPSSYST  
GVGFSPTQALKVPPLDQFPTFPPSAHQPPHYTTSAQQALLSPTPPDYTRHQQVPHILO  
GLLSPRHSLTGHSDIRLPTEFAQLIKRQQQQRQQQQQQQQQQQYQELFRHMNQG DAGSL  
APSLGGQSMTERQALS YQNADSYHHHTSPQHLLQIRAQECVSQASSPTPPHGYAHQPALM  
HSESMEEDCSCEGAKDGFQDSKSSSTLTGCHDSPLLLSTGGPGDPESLLGTVSHAQELG  
IHPYGHQPTAAFSKNKVPSREPVIGNCMDRSSPGQAVELPDHNLGLYPARPSVHEHHRPR  
ALQRHHTIQNSDDAYVQLDNLPGM SLVAGKALSSARMSDAVLSQSSLMGSQQFQDGENEE  
CGASLGGHEHPDLSDGSQHLNSSCYPSTCITDILLSYKHPEVSFSMEQAGV

SEQ ID NO: 153\_2R22-5-11\_H  
MTAVYMNGGGLVNP HYARWDRRDSVESGCQTESSKEGEEGQPRQLTPFEKLTQDMSQDEK  
VVREITLGKRIGFYRIRGEIGSGNFSQVKLGIHSLTKEKVAIKILDKTKLDQKTQRLLSR  
EISSMEKLHHPNIIRLYEVVETLSKLHLVMEYAGGGELFGKISTEGKLSEPESKLIFSQI  
VSAVKHMHENQIIHRDLKAENVFYTSNTCVKVGDFGFSTVSKKGEMLNTFCGSPPYAAPE

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## FIGURE 1H

LFRDEHYIGIYVDI WALGVLLYFMVTGTM PFRAETVAKLKKSILEGTYSVPPHVSEPCHR  
LIRGVLQQIPTERYGIDCIMNDEWMQGVPTPTLEPFQLDPKHLSETSTLKEEENEVKST  
LEHLGITEEHIRNNQGRDARSSITGVYRIILHRVQRKKALESVPMMLPDPKERDLKKGS  
RVYRGIRHTSKFCSIL

SEQ ID NO: 154\_R31237\_1\_H, AAC33487

MSTRTP LPTVNERDTENHTSHGDGRQEVTSRTSRSGARCRNSIASCAD EQPHIGNYRLLK  
TIGKGNFAKVKLARHILTGREVAIKIIDKTQLNPTSLQKLFREVRIMKILNHPNIVKLFE  
VIETEKTLYLIMEYASGGEVFDYLV AHGRMKEKEARSKFQIVSAVQYCHQKRIVHRDLK  
AENLLLDADMNIKIADFGFSNEFTVGGKLDTF CGSPPYAAPELFQGGKYDGPEVDVWSLG  
VILYTLVSGSLPFDGQNLKELRERVLRGKYRIPFYMSTDCENLLKRFLVLNPIKRGTLEQ  
IMKDRWINAGHEEDELKPFVEPELDISDQKRIDIMVGMGYSQEEIQESLSKMKYDEITAT  
YLLGRKSSSELDASDSSSSSNLSLAKVRPSSDLNNSTGQSPHHKVQRSVSSSQKQRRYS  
HAGPAIPSVVAYPKRSQTSTADGDLKEDGISSRKSSGSAVGKG IAPASPMLGNASNPKN  
ADIPERKKSSTVPSSNTASGGMTRRNTYVCSERTTADRHSVIQNGKENSTIPDQRTPVAS  
THSISSAATPDRI RFPRGTASRSTFHGQPRERRTATYNGPPASPSLSHEATPLSQTRSRG  
STNLFSKLTSKLTRSRNVSAEQKDENKEAKPRSLRFTWSMKTTSSMDPGDMMREIRKVLD  
ANNCDYEQRRERFLFCVHGDGHAENLVQWEMEVC KLPRLSLNGVRFKRISGTSIAFKNIA  
SKIANELKL

SEQ ID NO: 155\_W90839\_M

KGPSWSSRSLGARCRNSIASCPEEQPHVGN YRLLRTIGKGNFAKVKLARHILTGREVAIK  
IIDKTQLNPSSLQKLFREVRIMKGLNHPNIVKLFEVIETEKTLYLVMEYASAGEVFDYLV  
SHGRMKEKEARAKFRQIVSAVHYCHQKNIVHRDLKAENLLLD AEANI KIADFGFSNEFTL  
GSKLDTF CGSPPYAAPELFQGGKYDGPEVDIWSLG VILYTLVSGSLPFDGHNKELRERV  
LRGKYRVPFYMSTDCESILRRFLVLNPAKRCTLEQIMKDKWINIGYEGEELKPDTELKEE  
RMPGRKASCSAVGSGSRGLPPSSPMVSSAHNPKNKAEIPERRKDSTSTPNNLPPSMMTRN  
TYVCTERPGSERPSLLPNGKENSSGTSRVPPASPSHSLAPPSGERSRLARGSTIRSTFH  
GGQVRDRRAGSGSGGGVQNGPPASPTLAHEAAPLPSGRPRPTTNLFTKLTSKLTRRV TDE  
PERIGGPEVTSCHLPWDKTETAPRLLRFPWSVKLTSSRPS

SEQ ID NO: 156\_406786.5\_H

MEVGGLTVFEEDQRCLSQSLPLPVSAEGPAAQT TAEP SRSFSSAHRHLSRRNGLSRLCQS  
RTALSEDRWSSYCLSSLAAQNICTSKLHCPAAPEHTDPSEPRGSVSCCSLLRGLSSGWSS  
PLLPA PVCNPNKAI FTVD AKTTEILVANDKACGLLGYSQDLIGQKLTQFFLRSDSDVVE  
ALSEEHMEADGHA AVVFGTVVDIITRSGEKIPVSVWMKMRQERRLCCVVVLEPVERVST  
WVAFQSDGTITSCDSLFAHLHGYVSGEDVAGQHITDLIPSVQLPPSGQHIPKNLKIORSV  
GRARDGTTFPLSLKLKSQPSSEEATTGEAAPVSGYRASVWVFCTISGLITLLPDGTI HGI  
NHSFALT LFGYGKTELLGKNITFLIPGFYSYMDLAYNSSLQLPDLASCLDVGNESGCGER  
TLDPWQGDPAEGGQDPRINVVL AGGHVVP RDEIRKLMESQDI FTGTQTELIAGGQLLSC  
LSPQPAPGVDNVPEGSLPVHGEQALPKDQQIT ALGREEPVAIESPGQDLLGESRSEPVDV  
KPFASCEDSEAPVPAEDGGSDAGMCGLCQKAQLERMGVSGPSGSDLWAGAAVAKPQAKGQ  
LAGGSLLMHCPCYGSEWGLWWSQDLAPSPSGMAGLSFGTPTLDEPWLG VENDOR EELQTC  
LIKEQLSQLSLAGALDVPHAELVPTECQAVTAPVSSCDLGGRDLCGGCTGSSSACYALAT  
DLPGGLEAVEAQEVDVNSFSWNLKELFFSDQTDQTSSNCSCATSELRETPSSLAVGSDPD  
VGS LQEQGSCVLD DRELLLLTGTCVDLGQGRRFRESCVGHDPTEPLEVCLVSSEHYAASD  
RESPGHVPSTLDAGPEDTCPSAEPRNLNVQVTSTPVIVMRGAAGLQREIQEGAYSGSCYH  
RDGLRLSIQFEVRRVELQGPTPLFCCWL VKDLLHSQRDSAARTRFLASLPGSTHSTAAE  
LTGPSLVEVLRARPWFEEPPKAVELEGLAACEGEYSQKYSTMSPLGSGAFGFVWTAVDKG  
KNKEVVVKFIKKEKVLED CWIEDPKLGKVTLEIAILSRVEHANI I KVLDI FENQGFFQLV



## FIGURE 11

MEKHGSGLDLFAFIDRHPRLDEPLASYIFRQVRAGQSRLVSAVGYLRLKDI IHRDI KDEN  
 IVIAEDFTIKLIDFGSAAYLERGKLFYTFCGTIEYCAPEVLMGNPYRGPELEMWSLGVTLYTLVFEENPFCELEETVEAAIHPPYLVSKELMSLVSGLLQPVPERRTTLEKLVTDWPVWTQ  
 PVNLADYTWEVFRVKNKPESGVLSAASLEMGNRSLSDVAQAQELCGGPVPGEAPNGQGCL  
 HPGDPRLLTS

SEQ ID NO: 157\_AA544838\_M 406786\_M

TRPHPCLDPLASFIFRQLVSAVGYLHSQGI IHRDI KDENIVIAEDFTIKLIDFGSAAYL  
 ERGKLFYTFCGTIEYCAPEVLIGNPYRGPELEMWSLGVTLYTLIFEENPFCEVEETMEAV  
 IHPFVLVSQELMSLLSGLLQPCPEQRTTLEKLIRDPWVTQPVNLASYTWEVCRTNQPS  
 GLLSAASLEIGSRSPSEMAQREGLCGPPAPRETRGDQHCLHLKDPSPV

SEQ ID NO: 158\_AA785735\_H

MVMADGPRHLQRGPVVRVGFYDIEGTLGKGNFAVVKLGRHRITKTEVAIKI IDKSQLDVAVN  
 LEKIYREVQIMKMLDHPHI IKLYQVMETKSMYLVTEYAKNGEIFDYLANHGRLNESEAR  
 RKFWQILSAVDYCHGRKIVHRDLKAENLLLDNNMNIKIADFGFGNFFKSGELLATWCGSP  
 PYAAPEVFEGQQYEGPQLDIWSMGVVLVLCGALPFDGPTLPILRQRVLEGRFRI PYFM  
 SEDCEHLIRMLVLDPSKRLTIAQIKEHKWMLIEVPVQRPVLYPQEQENEPSIGEFNEQV  
 LRLMHS LGIDQQKXIESLQNKSYNHFAAIYFLLVERLKSHRSSFPVEQRLDGRQRRPSTI  
 AEQTVAKAQTVGLPVTMHSPNMRLLSALLPQASNVEAFSFPASGCQAEAAFMEEECVDT  
 PKVNGCLLDPPVPLVRKGCQSLPSNMETSIDEGLETEGEAEEDPAHAFAEFQSTRSGQ  
 RRHTLSEVTNQLVVMPGAGKIFSMNDSPSLSDVDSEYDMGSVQRDNLNLEDNPSLKDIML  
 ANQPSPRMTSPFISLRPTNPAMQALSSQKREVNHRSPVSFREGRRASDTSLTQGI VAFRQ  
 HLQNLARTKGILELNKVQLLYEQIGPEADPNLAPAAPQLQDLASSCPQEEVSQQQESVST  
 LPASVHPQLSPRQSLETQYLQHRLOKPSLLSKAQNTCQLYCKEPPRSLEQQQLQEHRLQOK  
 RLFLQKQSQLQAYFNQMQUIAESSYPQPSQQQLPLPRQETPPPSQQAPPFSLTQPLSPVLEP  
 SSEQMQYSPFLSQYQEMQLQPLPSTSGPRAAPPLPTQLQQQQPPPPPPPPPPRQPGAAPA  
 PLQFSYQTCELPSAASPAPDYPTPCQYPVDGAQQSDLTGPD CPRSPGLQEAPSSYDPLAL  
 SELPGLFDCEMLDAVDPQHNGYVLVN

SEQ ID NO: 159\_AA207220\_H

MESLVFARRSGPTPSAAELARPLAEGLIKSPKPLMKKQAVKRHHHKHNLRRHYEFLETLG  
 KGTYGKVKKARESSGRLVAIKSIRKDKIKDEQDLMHIRREIEIMSSLNHPHI IAIHEVFE  
 NSSKIVIVMEYASRGDLYDYI SERQQLSREARHFFRQIVSAVHYCHQNRVVHRDLKLEN  
 ILLDANGNIKIADFGLSNLYHQGKFLQTFCGSPLYASPEIVNGKPYTGPEVDSWSLGVLL  
 YILVHGTMFPDGHDKILVKQISNGAYREPPKPSDCLXGLIRWLLMVNPTRRATLEDVAS  
 HWWVNWGYATRVGEQEAPHEGGHPGSDSARASMA DWLRRSSRPLENGAKVCSFFKQHAP  
 GGGSTTPGLERQHSLKKSARKENDMAQSLHSDTADDTAHRPGKSNLKLKPKGILKKKVSASA  
 EGVQEDPPPELSPIPASPGQAAPLLPKKGILKKPRQRESGYSSPEPSESSEL LDAGDV FV  
 SGDPKEQKPPQASGLLLHRKGILKLNGKFSQTALELAAPTTFGSLDELAPPRPLARASRP  
 SGAVSEDSILSSESFDQLDLPERLPEPPLRGCVSDNLTGLEEPPSEGP GSCLRRWRQDP  
 LGDSCFSLTDCQEV TATYRQALRVCSKLT

SEQ ID NO: 160\_AA426580\_H, MAK\_V\_H

MPAAAGDGLLGEPAPGGGGGAEDAARPAACEGSFLPAWVSGVPRERLRDFQHHKRVGN  
 YLIGSRKLGEFSFAKVREGLHVL TGEKVAIKVIDKKRAKKDTYVTKNLRREGQIQQMIRH  
 PNITQLLDILETENSYYLVMELCPGGNLMHKIYEKKRLEESEARRYIRQLISAVEHLHRA  
 GVVHRDLKIENLLLEDNNIKLIDFGLSNCAGILGYSDPFSTQCGSPAYAAPELLARKKY  
 GPKIDVWSIGVNMYAMLTGTLPTVEPFSRLALYQKMVDKEMNPLPTQLSTGAISFLRSL  
 LEPDPVKRPNIQQALANRWLNENYTGVKPCNVTPNRI SLEDLSPSVVLHMTEKLGKNS



## FIGURE 1J

DVINTVLSNRACHILAIYFLLNKKLERYLSGKSDIQDSLQCYKTRLYQIEKYRAPKESYEA  
SLDTWTRDLEFHAVQDKKPKEQEKRGDFLHRPFSKKLDKNLPSHKQPSGSLMTQIQNTKA  
LLKDRKASKSSFPDKDSFGCRNIFRKTSDSNCVASSSSMEFIPVPPPTPRIVKKPEPHQF  
GPGSTGIPHKEDPLMLDMVRSFESVDRDDHVEVLSPSHHYRILNSPVSLARRNSSERTLS  
PGLPSGSMSP LHTPLHPTLVSF AHEDKNSPPKEEGLCCPPPVPSNGPMQPLGSPNCVKSR  
GRFPMMGIGQMLRKRHQSLQPSADRPLEASLPPLQPLAPVNLAFDMADGVKTQC

SEQ ID NO: 161\_Z36720\_H

MDTKLNMLNEKVDQLLHFQEDVTEKLQSMCRDMGHLERGLHRLEASRAPGPGGADGVPHI  
DTQAGWPEVLELVRAMQQDAAQHGARLEALFRMVA AVDRAIALVGATFQKSKVADFLMQG  
RVPWRRGSPGDSPEEWVKEEEVCFMPPVPPAPGAAGQSLQKDKGELS AEQGIWATLMTLV  
IMVTAANKERVEEEGGKPKHVLSTSGVQSDAREPG EESQKADVLEGTAERLPPIRASGLG  
ADPAQAVVSPGQGDGVPGAQAFPGHLPLPTKVEAKAPETPSENLR TGLELAPAPGRVNV  
VSPSLEVAPGAGQGASSSRPDPEPLEEGTRLTPGPGPQCPGPPGLPAQARATHSGGETPP  
RAALLKGAVAPGFSRRDLVFPSIFCACLGISIHQEMDTPGEMLM TGRGSLGPTLTTEAP  
AAAQPGKQGPPTGRCLQAPGTEPGEQTPEGARELSPLQESSSPGGVKAEEEEQRAGAEFG  
TRPSLARSDDNDHEVGALGLQQGKSPGAGNPEPEQDCAARAPVRAEAVRRMPPGAEGSV  
VLDDSPAPPAPFEHRVSVKETSISAGYEVCQHEVLGGGRFGQVHRCTEKSTGLPLAAKI  
IKVKSADREDVKNEINIMNQLSHVNLIQLYDAFESKHSCTLM EYVDGGELFDRITDEK  
YHLTELDVVLFTTRQICEGVHYLHQHYILHLDLKPENILCVNQTGHQIKIIDFGLARRYKP  
REKLKVNFGTPEFLAPEVVNYEFVSFPTDMWSVG VITYMLLSGLSPFLGETDAETMNFIV  
NCSWDFDADTFEGLSEEAKDFVSRLLVKEKSCRMSATQCLKHEWLNNLPAKASRSKTRLK  
SQQLLQKYIAQRKWKKHFYVVTAANRLRKFTSP

SEQ ID NO: 162\_SGK088\_H

GEMALFECLVAGPTDVEVDWLCRGRLLQPALLKCKMHFDGRKCKLLLT SVHEDDSGVYTC  
KLSTAKDELTC SARLTVRPSLAPLFTRLLEDVEVLEGRAARFDCKISGT PPPVVTWTHFG  
CPMEESENRLRQDGGHLHSLHIAHVGESEDEGLYAVSAVNTHGQAHC SAQLYVEEPRTAAS  
GPSSKLEKMPSIPEEPEQGELERLSIPDFLRPLQDLEVGLAKEAMLECQVTGLPYPTISW  
FHNGHRIQSSDDRRMTQYRDVHRLVFP AVGPQHAGVYKSVIANKL GKAAACYAHLYVTDVV  
PGPPDGAPQVVAVTGRMVTLTWNPPRSLDMAIDPDSLTYTVQH QVLSGSDQWTALVTGLRE  
PGWAATGLRKG VQHIFRVLSTTVKSSSKPSPSEP VQLLEHGPTLEEAPAMLDKPDIVYV  
VEGQPASVTVTFNHVEAQVWVRSCRGALLEARAGVYELS QPDDDQYCLRICRVSRDMGA  
LTCTARNRHGTQTCSVTLELAEAPRFESIMEDVEVGAGETARFAVVVEGKPLPDIMWYKD  
EVLLTESSHVSFVYEENECSLVVLSTGAQDGGVYTCTAQNLAGEV SCKAELAVHSAQTAM  
EVEGVGEDEDHRGRRLSDFYDIHQEIGRGAFSYLRRIVERSSGLEFAAKFIPSQAKPKAS  
ARREARLLARLQHDCVLYFHEAFERRRGLVIVTELCTEELLERIARKPTVCESEIRAYMR  
QVLEGIHYLHQSHVLHLDVKPENLLVWDGAAGEQQVRI CDFGNAQELTPGEPQYCQYGTP  
EFVAPEIVNQSPVSGVTDIWPVG VVAFLCLTGISPFVGENDR TTMNIRNYNVAFEETTF  
LSLSREARGFLIKVLVQDRLRPTAEETLEHPWFKTQAKGAEVSTDHLKLFLSRRRWQRSQ  
ISYKCHLVLRPIPELLRAPPERVWVTMPRRPPPSGGLSSSSDSEEELEELPSVPRPLQP  
EFSGSRVSLTDIPTED EALGTPETGAATPMDWQEQGRAPSQDQEAPSPEALPSPGQEPAA  
GASPRRGELRRGSSAESALPRAGPRELGRGLHKAASVELPQRRSPGPGATRLARGGLGEG  
EYAQRLQALRQRLLRGGPEDGKVSGLRGPLESLGGRARDPRMARAASSEAAPHHQP PLE  
NRGLQKSSSFSGGEAEPRGRHRRAGAPLEIPVARLGARRLQESPSLSALSEAQPSSPARP  
SAPKPSSTPKSAEPSATTPSDAPQPPAPQPAQDKAPEPRPEPV RASKPAPPPQALQTLALP  
LTPYAQIIQSLQLSGHAQGPSQGPAAPPSEPKPHA AVFARVASPPPGAPEKRVPSAGGPP  
VLAEKARVPTVP PRPGSSLSSSIENLESEAVFEAKFKRSRESPLSLGLRLLSRSRSEERG  
PFRGAEEEDGIYRPSAGTPLELVRRPERSRSVQDLRAVGEPGLVRRLSLSLSQRLR RTP  
PAQRHPAWEARGGDGESSEGGSSARGSPVLAMRRRLSFTLERLSSRLQRSGSSEDSGGAS

## FIGURE 1K

GRSTPLFGRLRRATSEGESLRRRLGLPHNQLAAQAGATTPSAESLGSEASATSGSSAPGES  
 RSRLRWGFSRPRKDKGLSPPNLSASVQEELGHQYVRSESDFPVFHIKLKDQVLLEGEAA  
 TLLCLPAACPAPHISWMKDKKSLRSEPSVIIVSCKDGRQLLSIPRAGKRHAGLYECSATN  
 VLGSITSSCTVAVARVPGKLAPPEVTQTYQDTALVLWKPGDSRAPCTYTLERRVDGESVW  
 HPVSSGIPDCYYNVTHLPVGVTVRFRVACANRAGQGPFSSNSSEKVFVRGTQDSSAVPSAA  
 HOEAPVTSRPARARPPDSPTSLAPPLAPAAPTPPSVTVSPSSPPTPPSQALSSLKAVGPP  
 PQTPPRRHRGLQAARPAEPTLPSTHVTPEPKPFVLDGTPIIPASTPQGVKPVSSSTPVY  
 VVTSFVSAPPAPPEPPAPEPPPEPTKVTVQSLSPAKEVVSSPGSSPRSSPRPEGTTLRQGP  
 PQKPYTFLEEKARGRFGVVRACRENATGRTFVAKIVPYAAEGKPRVLQEYEVLRTLHHER  
 IMSLHEAYITPRYLVLIAESCGNRELLCGLSDRFRYSEDDVATYMVQLLQGLDYLHGHHV  
 LHLDIKPDNLLLAPDNALKIVDFGSAQPYNPQALRPLGHRTGTLEFMAPEMVKGEPISGA  
 TDIWGAGVLTYIMLSGRSPFYEPDPQETEARIVGGRFDAFQLYPNTSQSATLFLRKVLSV  
 HPWSRPSLQDCLAHPWLQDAYLMKLRRQTLTFTTNRLKEFLGEQRRRRRAEAATRHKVLLR  
 SYPGGP

SEQ ID NO: 163\_AA542015\_M SGK088\_M

ATDIWGAGVLTYIMLSGYSPFYEPDPQETEARIVGGRFDAFQLYPNTSQSATLFLRKVLS  
 VHPWSRPSLQDCLAHPWLQDAYLMKLRRQTLTFTTNRLKEFLGEQRRRRRAEAATRHKVLL  
 RSYPGSP

SEQ ID NO: 164\_R19772\_H

MKGGDRAYTRGPSLGWLFACCCCCFPCRDAYSHSSSENGGKSESVANLQAQPSLNFIHSS  
 PGPKRSTNTLKKWLTSPVRRNLNSGKADGNIKKQKKVRDGRKSFDLGSPKPGDETTPQGDS  
 ADESKKGWGEDEPDEESHTPLPPPMKIFDNDPTQDEMSSSLAARQASTEVPATAADLVNA  
 IEKLVKNKLSLEGSSYRGSLKDPAGCLNEGMAPPTPPKNPEEEQKAKALRGRMFVLNELV  
 QTEKDYVKDLGIVVEGFMKRIEEKGVPEDMRGKDKIVFGNIHQIYDWHKDFFLAELEKCI  
 QEODRLAQLFIKHERKLHIYVWYCQNKPRSEYIVA EYDAYFEEVKQEINQRLTSLDFLIK  
 PIQRITKYQLLLKDFLRYSEKAGLECS DIEKAVELMCLVPKRCNDMMNLGRLQGFEGTLT  
 AOGKLLQQDTFYVIELDAGMQSRTKERRVFLFEQIVIFSELLRKGS LT PGYMFKRSIKMN  
 YLVLEENVNDNDPCKFALMNRETSE RVVLQAANADIQQAWVQDINQVLETQRDFLNALQSP  
 IEYQRKERSTAVMRSQPARLPQASPRPYSSVPAGSEKPPKGSSYNPPLPPLKISTSNNGSP  
 GFEYHQPGDKFEASKNDLGGCNGTSSMAVIKDYYALKENEICVSQGEVVQVLAVNQONMC  
 LVYQPASDHSPAAEGWVPGSILAPLTKATAAESDGSIKKSCSWHTLRMRKRAEVENTGK  
 NEATGPRPKPDILGNKVS VKETNSSESEECDDLDPNTSMEILNPNFIQEVAPEFLVPLVD  
 VTCLLGDTVILQCKVCGRPKPTITWKGPDQNI LDTDNSSATYTVSSCDSGEITLKI CNLM  
 PQDSGIYTCIATNDHGTSTSATVKVQGVPAAPNRPIAQERSCTSVILRWLPPSSSTGNCT  
 ISGYTVEYREEGSQIWQQSVASTLD TYLVIEDLSPGCPYQFRVSASNPWGISLPSEPSEF  
 VRLPEYDAAADGATISWKENFDSAYTELNEIGRGRFSIVKKCIHKATR KDVAVKFVNKKM  
 KKKEQAAHEAALLQHLQHPQYITLHDTYESPTS YILILELMDDGRLLDYLMNHDELMEEK  
 VAFYIRDIMEALQYLHNCRVAHLDIKPENLLIDLRI PVPRVKLIDLEDAVQISGHFHIHH  
 LLGNPEFAAPEVIQGI PVSLGTDIWSIGVLTYVMLSGVSPFLDESKEETCINVCRVDFS F  
 PHEYFCGVSNAARDFINVILQEDFRRRPTAATCLQHPWLQPHNGSYSKIPLDTSRLACFI  
 ERRKHQNDVRPIPNVKS YIVNRVNQGT

SEQ ID NO: 165\_5R72\_8\_2\_H

MADSGLDKKSTKCPDCSSASQKDVLCVCSSKTRVPPVLVVEMSQTSSIGSAESLISLERF  
 KEKNINRDITSRKDLPSRTSNVERKASQQQWGRGNFTEGKVPHIRIENGAAIEEIYTFGR  
 ILGKGSFGIVIEATDKETETKWA I KKNKEKAGSSAVKLLEREVNILKSVKHEHI IHLEQ  
 VFETPKKMYLVMELCEDGELKEILDRKGHFSENETRWIIQSLASAIAYLHNNDIVHRDLK  
 LENIMVKSSLIDDNNEINLNIKVTD FGLAVKKQSRSEAMLQATCGTPIYMAPEVISAHDY

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## FIGURE 11.

SQQCDIWSIGVVMYMLLRGEPFLASSEAKLFELIRKGE LHFENAVWNSISDCAKSVLKQ  
LMKVDPAHRI TAKELLDNQWLTGNKLSSVRPTNVLEMMKEWKNNPESVEENTTEEKNKPS  
TEEKLKSYQPWGNVPETNYTSDEEEEEKQSTAYEKQFPATSKDNFDMCSSSFTSSKLLPAE  
IKGEMEKTPVTPSQGTATKYPAKSGALSRTKKKL

SEQ ID NO: 166\_SGK309\_H

MQCLAAALKDETNMSGGGEQADILPANYVVKDRWKVLKKIGGGGFGEIYEAMDLLTREN  
ALKVESAAQQPKQVLKMEVAVLKKLQGSGLGQGDGKEEMMKPGAKRGKDHVCRFIGCGRNE  
KFNYVVMQLQGRNLADLRRSQPRGTFTLSTTLRLGKQILESEIAIHSVGF LHRDIKPSNF  
AMGRLPSTYRKCYMLDFGLARQYTNTTGDVRPPRNVAGFRGTVRYASVNAHKNREMGRHD  
DLWSLFYMLVEFAVGQLPWRKIKDKEQVGMKEKYEHRMMLLKHMPSEFHLFLDHIASLDY  
FTKPDYQLIMSVFENSMKERGIAENEAFDWEKAGTDALLSTSTSTPPPAEHPADGSHVWG  
GQCDASAWGPAPGEHRGCATGRAPEXPGECTPNSAREALXGAGPQSPPCPPPRGSXGXSL  
GGDRCQPEQTPDQHRQSNCRQGEGRGWPF LSPPIPSLVPLPCSSXAPCPPPI SLLARPLF  
PVPSPALASLCLPSSSSSVSFTLRRPSA

SEQ ID NO: 167\_AA234451\_H

MSGGGEQLDILSVGILVKERWKVLRKIGGGGFGEIYDALDMLTRENVALKVESAAQQPKQV  
LKMEVAVLKKLQGDHVC RFIGCGRNDRFNYVVMQLQGRNLADLRRSQSRGTFTISTTLR  
LGRQILESEIHSVGSXHRDIKPSNFAMGRFPSTCRKCYMLDFGLARQFTNSCGDVRPP  
RAVAGFRGTVRYASINAHNRNREMGRHDDLWSLFYMLVEFVVGQLPWRKIKDKEQVGSIKE  
RYDHRLMLKHLPPFEFSIFLDHISSLDYFTKPDYQLLTSVFDNSIKTFGVIESDPFDWEKT  
GNDGSLTTTTTTSTTPQLHTRLTPAAIGIANATPIPGDLLRENTDEVFPDEQLSDGENGIP  
VGVSPDKLPGSLGHPRPQEKDVWEEMDANKNKIKLGICKAATEEENSHGQANGLLNAPSL  
GSPIRVRSEITQPDRDIPLVRKLRSIHSFELEKRLTLEPKPDTDKFLETWYKIVYFSF

SEQ ID NO: 168\_AA435956\_H

TFTIFFEMTVFDLEAKSARGGSNLLMDSVSSFQLFMFQLLRGLAYIHHQHVLHRDLKPQN  
LLISHLGELKLADFGLARAKSIPSQTYSSSEVVT LWYRPPDALLGATEYSSELDIWGAGCI  
FIEMFQGQPLFPGVSNILEQLEKIWEVLGVPTEDTWPGVSKLPNYPNPEWFPLPTPRSLHV  
VWNRLGRVPEAEDLASQMLKGFPRDRVSAQEALVHDYFSALPSQLYQLPDEESLFTVSGV  
RLKPEMCDLLASYQKGHHPAQFSKCW

SEQ ID NO: 169\_AA626859\_H

NGVADGVIKSVLWQTLQALNFCHIHNCIHRDIKPENILITKQGIKICDFGFAQILIPGD  
AYTDYVATRWRAPPELLVGDTQYGSSVDIWAIGCVFAELLTGQPLWPGKSDVDQLYLIIR  
TLGKLI PRHQSI FKSNGFFHGISIPEPEDMETLEEKFSVDVHPVALNFMKGCLKMNPDDR  
TCSQLLESSYFDSFQEAQIKRKARNEGRNRRRQQNQLLPLIPGSHISPTPDGRKQVLQK  
FDHLPNI

SEQ ID NO: 170\_AA061797\_M

KIALREIRMLKLKHPNLVNLIEVFRRKRKMHLVFEYCDHTLLNELERNPNNGVSDGVIKSV  
LWQTLQALNFCHKHNCIHRDVKPENILITKQGMKICDFGFARILIPGDAYTDYVATR  
WRAPPELLVGDTKYGSSVDVWAVGCVFAELLTGQPLWPGKSDVDQLYLIIRTLGKLI PRHQ  
SIFRSNQFFRGISIPEPEDMETLEEKFSNVQPVALSFMKGCLKMNPDERLTCAQLLDSAYF  
ESFQEDQMKRKARSEGRSRRRQQNQLLPLIPGSHISPTPDGRKQVVQLKFDHLPNI

SEQ ID NO: 171\_AA397553\_H

MPNSERHGGKKGSGGASGTLQPSSGGGSSNSRERHRLVSKHKRHKSKHSDMGLVTPEA  
ASLGTVIKPLVEYDDISSDSTFSDDMAFKLDRRENDERRGSDRSDRLHKHRHHQHRRSR

## FIGURE 1M

DLLKAKQTEKEKSQEVSSKSGSMKDRI SGSSKRSNEETDDYGKAQVAKSSSKESRSSSKLH  
 KEKTRKERELKSGHKDRSKSHRKRETPKSYKTVDSPKRRSRSPHRKWSDDSSKQDDSPSGA  
 SYGQDYDLSPSRSHTSNYDSYKKSPGSTSRRQSVSPPYKEPSAYQSSTRSPSPYSRRQR  
 SVSPYSRRRSSSYERSGSGSYGRSPSPYGRRRSSSPFLSKRSLSRSPPLPSRKSMKSRSRSP  
 AYSRHSSSHSKKKRSSSRSRHSSI SPVRLPLNSSLGAELSRKKKERAAAAAAAKMDGKES  
 KGSPVFLPRKENSSVEAKDSGLESKKLPRSVKLEKSAPDTELNVNTHLNTDEVKNSSDTGK  
 VKLDENSEKHLVKDLKAQGTRDSKPIALKEEIVTPKETETSEKETPPPLPTIASPPPLP  
 TTTPPPQTPPLPPLPPI PALPQQPPLPPSQPAFSQVPASSTSTLPPSTHSKTSASVSSQAN  
 SQPPVQVSVKTQVSVTAAI PHLKTSTLPPPLPPLLPGGDDMDSPKETLPSKPKVKEKEQ  
 RTRHLLTDLPLPELPGGDLSPDSEPKAITPPQQPYKKRPKICCPRYGERRQTESDWG  
 KRCVDKFDI IGI IEGTYGQVYKARDKDTGELVALKKVRLDNEKEGFPITAI REIKILRQ  
 LIHRSVVMKEIVTDKQDALDFKKDKGAFYLVFEYMDHDLMLGLESGLVHFSEDHI KSF  
 KQLMEGLEYCHKKNFLHRDIKCSNILLNNSGQIKLADFGGLARLYNSEESRPYTNKVITLW  
 YRPPPELLLGEERYTPAIDVWSCGCILGELFTKKPIFQANLELAQLELISRLCGSPCPAVW  
 PDVIKLPYFNTMKPKKQYRRRLREEFSFI PSAALDLLDHMLTLDP SKRCTAEQTLQSDFL  
 KDVELSKMAPPDLPHWQDCHELWSKKRRRQRQSGVVVEEPPPSKTSRKETTSGTSTEPVK  
 NSSPAPPQPAPGKVESGAGDAIGLADITQQLNQSELAVLLNLLQSQTDL SI PQMAQLLNI  
 HSNPEMQQQLALNQSISALTEATSQQQDSETMAPEESLKEAPSAPVILPSAEQMTLEAS  
 STPADMQNILAVLLSQLMKTQEPAGSLEENNSDKNSGPQGRRTPTMPQEEAAACPPHIL  
 PPEKRPPEPPGPPPPPPPPPLVEGDLSSAPQELNPAVTAALLQLLSQPEAEPPGHLPH  
 QALRPMEYSTRPRPNRTYGN TDGPETGFS AIDTDERN SGPALTESLVQTLVKNRTFSGSL  
 SHLGESSSYQGTGSVQFPGDQDLRFARVPLALHPVVGQPF LKAEGSSNSVVHAETKLQNY  
 GELGPGTTGASSSGAGLHWGGPTQSSAYGKLYRGPTRVPPRGGRGRGV PY

SEQ ID NO: 172\_AA789239\_H

MEMYETLGKVGEGSYGTVMKCKHKNTGQIVAIKIFYERPEQSVNKIAMREIKFLKQFHHE  
 NLVNLI EVFRQKKKIHLVFEFIDHTVLDELQHYCHGLESKRRLKYL FQILRAIDYLHSNN  
 V IHRDIKPENILVSQSGITKLCDFGFARTLAAPGDIYTDYVATRWRAPELVLKDTSYG  
 KYVPVDI WALGCM IEMATGNPYLPSSSDLDLLHKIVLKVXFMP ELKAKLLQEAKVNSLI  
 KPKESSKENELRKDERKTVYTNTLLSSSVLGKEIEKEKKPKEIKVRVIKVKGGRGDI SEP  
 KKKEYEGGLGQQDANENVHPMSPDTKLVTIEPPNPINPSTNCNGLKENPHCGGSVTMPPI  
 NLTNSNLMAANLSSNLFHPSVRLTERAKKRRTSSQSIGQVMPNSRQEDPGPIQSOMEKGI  
 FNERTGHSDQMANENKRKLNF SRSDRKEFHFP ELPVTIQSKDTKGMEVKQIKMLKRESKK  
 TESSKIPTLLNVDQNEKQEFIPLSLLSACCPIFTNICSQLTIRVEMAIARGRI

SEQ ID NO: 173\_AA124976\_M

LADIVHACLQIDPAERTSSTDLLRHDFTRDGFIEKFIP ELRAKLLQEAKVNSFIKPKEN  
 FKENEPVRDEKKS VFTNTLLYGNPSLYGKEVD RDKRAKELKVRVIKAKGGKGDVPDQKKP  
 EYEGDHRQQGTADDTQPSSLDKKPSVLELTNPLNPSSENSDGVKEDPHAGGCMIMPPINLT  
 SSNLLAANLSSNLSHPNSRLTERTKKRRTSSQTIGQTLNSNRQEDTGPTQVQTEKGAFNE  
 RTGQNDQISSGNKRKLNF PKCDRKEFHFP ELPFTVQAKEMKGMEVKQIKVLKRESKKTDS  
 SKIPTLLSMDPNQEKQEGGDGDCEGKNLKRNRFFFSR

SEQ ID NO: 174\_AA575635\_M CCRK\_M

SASGQLKIADFGGLARVFS PDGGRLYTHQVATRWRAPELLYGARQYDQGVDLWAVGCIMG  
 ELLNGSPLFPGENDIEQLCCVLRILGTPSPRVWPEITELPDYNKISFEEQAPVPLEEVLP  
 DASPQALDLLGQFLLYPPRQRIAASQALLHQYFFTAPLPAHPSELPIPQRPGGPAPKAHP  
 GPPHVHDFHVDRPIEESLLNPELIRPFIPEG



## FIGURE 1N

SEQ ID NO: 175\_AA631990\_H

MIT SISTE KSGH THYP FMIT TLQYYRGRGGKTAVWRHFS AEGPFAFAEMRHSKRTHCPDW  
DSRESWG HESYRGSHKRKRSHSSTQENRHCKPHHQFKESDCHYLEARSLNERDYRDRRY  
VDEYRNDYCEGYVPRHYHRDIESGYRIHCSKSSVRSRRSSPKRKRNRHCSSHQSR SXEIV  
DTLGEGAFGKVVECIDHGMDGMHVAVKIVKNVGRYREARSEIQVLEHLNSTDPNSVFR  
VQMLEWFDHHGHVCIVFELLGLSTYDFIKENSFLPFQIDHIRQMAYQICQSINFLHHNKL  
THTDLKPENILFVKSDYVVKYNSKMKRDER TLKNTDIKVVD FGSATYDDEHHSTLVSTRH  
YRAPEVILALGWSQPCDVWSIGCILIEYYLGFTVFQTHDSKEHLAMMERILGP I PQHMIQ  
KTRKRKYFHHNQLDWDEHSSAGRYVRRRCKPLKEFMLCHDEEHEKLFDLVRRMLEYDPTQ  
RITLDEALQHPFFDLLKKK

SEQ ID NO: 176\_AA557536\_H

MCTVVDPRIVRRYLLRRQLGQGRTFREITLLQVSGLGPPVQSPCPGTDLSRQERNWPSWA  
PEHSPSWPSSRLRLSPQEFGDHPNIIISLLDVIRAENDRDIYLVFEFMDTDLNAVIRKGG  
LQDVHVR SIFYQLLRATRFLHSGHVVRDQKPSNVLLDANCTVKLCDFGLARSLGDLPEG  
PEDQAVTEYVATR WYRAPEVLLSSHRYTASCPRYTLGVDMWSLGCILGEMLRGRPLFPGT  
STLHQLELILETIPPPSEEXRPRQTL DALLPPDTSPEALDLLRRLLVFAPDKRLSATQAL  
QHPYVQRFHCP SDEWAREADVPR AHEGVQLSVPEYRSRVYQMI LECGGSSGTSREKGPE  
GVSPSQ AHLHKPRADPQLPSRTPVQGPRPRPQSSPGHDP AEHESPRAAKNVPRQNSAPLL  
QTALLNGERPPGAKEAPPLTSLVKPSGRGAAPSLTSQAAAQVANQALIRGDWNRGGGV  
RVASVQQVPPRLPPEARPGRRMFSTSALQGAQG GARALLGGYSQAYGTVCHSALGHLPLL  
EGHHV

SEQ ID NO: 177\_N28606\_H, MOK\_H

MKNYKAIGKIGEGTFSEVMKMQLRDNYYACKQMKQRFESIEQVNNLREIQALRRLNPH  
PNILMLHEVVFD RKSGSLALICELMDMNIYELIRGRRYPLSEKKIMHYMYQLCKSLDHIH  
RNGIFHRDVKPENILIKQDVLKLGDFGSCRSVYSKQPYTEYISTRWYRAPECLLTDGFYT  
YKMDLWSAGCVFYEIASLQPLFPGVNELDQISKIHDVIGTPAQKILTKFKQSRAMNFDFF  
FKKGS GIPLLTTNLS PQCLSLHAMVAYDPDERIAAHQALQHPYFQEQRKTEKRALGSHR  
KAGFPEHPVAPEPLSNSCQISKEGRKQKQSLKQEEDRPKRRGPAYVMELPKLKL SGVVRL  
SSYSSPTLQSVLGS GTNGRVPVLRPLKCI PASKKTD POKDLKPAPQQCRLPTIVRKGG

SEQ ID NO: 178\_AB023153\_H, ICK\_H

MNRYTTIRQLGDGT YGSVLLGRSIESGELIAIKMKRKFYSWEECMNQREV KSLKKNLHA  
NVVKLKEVIRENDHLYFIFEYMKENLYQLIKERNKLPESAIRNIMYQILQGLAFIHKLG  
FFHRDLKPENLLCMGP ELVKIADFGlareIRSKPPYTDYVSTRWYRAPEVLLRSTNYSSP  
IDVWAVGCIMAEVYTLRPLFP GASEIDTIFKICQVLGTPKKTDWPEGYQLSSAMNFRWPQ  
CVPNNLKTLPNASSEAVQLLRDMLQWDPKKRPTASQALRYPYFQVGHPLGSTTQNLQDS  
EKPQKGILERAGPPPYIKPVPPAQPPAKPHTRISSRQH QASQPPLHLTPYKAEVSRTDH  
PSHLQEDKPSPLLP SLHNKHPQSKITAGLEHKNGEIKPKSRRRWGLISRSTKDSDDWAD  
LDDLD FSPSLSRIDLKNKKRQSDDTL CRFESVLDLKPSEPVG TGN SAPTQTSYQRRDTPT  
LRSAAKQHLYLKHSRYLPGISIRNGILSNPGKEFIPPNPWSSSGLSGKSSGTMSVISKVNS  
VGSSSTSSSGLTGN YVPSFLKKEIGSAMQRVHLAPIPDPSPGYSSLKAMRPHPGRPFLDT  
QPRSTPGLIPRPPAAQPVHGRTDWASKYPSRR

SEQ ID NO: 179\_AA839940\_M

SSNNGGMSAEEEEIGPGAEPMRGPSLATRDWRDET VGT TDLQQGIDPGAVSPEPGKDHA AQ  
GPGRTEAGRVSSAAEAAIVVLDDSAAPPAPFEHRVVS IKDTLISAGYTVSQHEVLGGGRF  
GQVHRCTERSTGLALAAKIIKVKNVKDREDVKNEVNIMNQLSHVNLIQLYDAFESKNSFT  
LIMEYVDGGELFDRITDEKYHLTELDVVLFT RQICEGVHYLHQHYILHLDLKPENILCVS



## FIGURE 10

QTGHQIKI IDFG LARRYKPREKLKVNFGTPEFLAPEVVNYEFVSFPTDMWSVGVITYMLL  
SGLSPFLGETDAETMNFIVNCSWDFDADTFKGLSEEAKDFVSRLLVKEKSCRMSATQCLK  
HEWLNHLPAKASGSNVRLRSQQLLOKYMAQSKWKKHFHVVA AVNRLRKFP TCP

SEQ ID NO: 180\_AA460132\_H

MAAARATTPADGEEPAPAEALAAARERSRFLSGLELVKQGAEARVFRGRFQGRAAVIK  
HRFPKGYRHPALEARLGRRTVQEARALLRCRRAGISAPVVFVDYASNCLYMEEIEGSV  
TVRDYIQSTMETEKTPQGLSNLAKTIGQVLARMHDEDLIHGDLTTSNMLLKPPLEQLNIV  
LIDFGLSFISALPEDKGVLDLYVLEKAF LSTHPNTETVFEAF LKSYSTSSKKARPVLKKLD  
EVRLRGRKRSMVG

SEQ ID NO: 181\_SGK034\_H

QREKVNQGNMPGLQSTFLAMDTEEGVEVVWNLHFGDRKAFAAHEEKIQTVFEQLVLVDH  
PNIVKLHKYWLDTSEACARVIFITEYVSSGSLKQFLKKTCKNHKAMNARAWKRWCTQILS  
ALSFLHACSPPIIHGNLTSDTIFIQHNGLIKIGSVWHRIFSNALPDDLRSPIRAEREELR  
NLHFFPPEYGEVADGTAVDIFSFGMCALEMAVLEIQTNNGDTRVTEEA IARARHSLSDPNM  
REFILCCLARDPARRPSAHSLLFHRVLF EVHSLKLLAAHCFIQHQY LMPENVVEEKTAM  
DLHAVLAELPRPRRPPLQWRYSEVSFMELDKFLEDVRNGIYPLMNFAATRPLGLPRVLAP  
PPEEVQKAKTPTPEPFDSETRKVIQMOCNLERSEDKARWHLTLLLVL EDRLHRQLTYDLL  
PTDSAQDLASELVHYGFLHEDDRMKLA AFLESTFLKYRG TQA

SEQ ID NO: 182\_AA103218\_M SGK034\_M

HASAPEYGEVNDGTGFVDIFSFGMCALEMAVLEIQANGDTRVTEEA IARARHSLSDPNMR  
EFILSCLARDPARRPSAHNLLFHRVLF EVHSLKLLAAHCFIQHQY LMPENVVEEKTAM  
LHAVLAEMPQPHGPPMQWRYSEVSFLELDKFLEDVRNGIYPLMNFAAARPLGLPRVLAPP  
PEEAQKAKTPTPEPFDSETRKVVQMOCNLERSEDKARWHLTLLLVL EDRLHRQLTYDLLP  
TDSAQDLAAELVHYGFLHEDDRTKLA AFLETTFLKYRG TQA

SEQ ID NO: 183\_NEK7\_H, N34132\_H

MSGGAAEKQSSTPGSLFLSPAPAPKNGSSSDSSVGEKLGAAAADAVTGRTEEYRRRRHT  
MDKDSRGAAATTTTTEHRFFRRSVICDSNATALELPGLPLSLPQPSI PAAVPQSAPPEPH  
REETVTATATSQVAQQPPAAAAPGEQAVAGPAPSTVPSSTSKDRPVSQPSLVGSKEEPPP  
ARSGSGGGSakePQEERSQQQDDIEELET KAVGMSNDGRFLKFDIEIGRGSFKTVYKGLD  
TETTVEVAWCELQDRKLT KSERQRFKEEAEM LKGLQHPNIVRFYDSW ESTVKGKKCIVLV  
TELMTSGTLKTYLKRFKVMKIKVLRSWCRQILKGLQFLHTRTPLI IHRDLKCDNIFITGP  
TGSVKIGDLGLATLKRASFASVIGTPEFMAPEMYEEKYDESVDVYAFGMCMLEMATSEY  
PYSECQNAAQIYRRVTSGVKPASFDKVAIPEVKEIIEGCIRQNKDERYSIKDLLNHAFQ  
EETGVRVELAEEDDGEKIAIKLWLRIEDIKKLKGKYKDNEAIEFCFDLERDVPEDVAQEM  
VESGYVCEGDHKTMAKAIKDRVSLIKRKREQRQLVREEQENKKQEESLKKQQVEQSSASQ  
TGIKQLPSASTGIPTASTTSASVSTQVEPEEPEADQHQQQLQYQQPSISVLS DGTVD SGQG  
SSVFTESRVSSQQT VSYGFPXHEQAHSTGTVP GHI PSTVQAQSQPHGVYPPSSVQOGIQQ  
TAPPQQT VQYSLSQTSTSS EATTAQPV SQPQAPQVLPQVSAGKQSTQGV SQVAPAE PVAV  
AQ PQATQPTTLASSVDSAHSDVASGMSDGNENVPSSSGRHEGRTTKRH YRKS VRSR SRHE  
KTSRPKLRI LNVSNKGDRVVECQLETHNRKMVTFKFDLDGDNPEE IATIMVNNDFILAE  
RESFVDQVREIIEKADEMLSEDVSVEPEGDQGLES LQGKDDYGFSGSQKLEGEFKQPIPA  
SSMPQQIGIPTSSLTQVVHSAGRRFIVSPVPESRLRESKVFPSEITDTVAASTAQSPGMN  
LSHSASSLSLQQAFSELRR AQMTEGPNTAPPNFSHTGPTFPVVPFLSSIAGVPTTAAAT  
APVPATSSPPNDISTSVIQSEVTVPTEEGIAGVATSTGVVTSGGLPIPPVSESPVLSSVV  
SSITIPAVVSISTTSPSLQVPTSTSEIIVVSSTALYPSVTVSATSASAGGSTATPGPKPPA  
VVSQQAAGSTTVGATLTSVSTTTSPSTASQLSIQLSSSTSTPTLAETVVVSAHSLDKTS

## FIGURE 1P

HSSTTGLAFSLSAPSSSSSPGAGVSSYISQPGGLHPLVIPSVIASTPILPQAAGPTSTPL  
 LPQVPSIPPLVQPVANVFAVQQTLIHSQPPALLPNQPHTHCPEVDSDTQPKAPGILDJIK  
 TLEEKLRSLFSEHSSSGAQHASVSLETSLVIESTVTPGIPTTAVAPSKLLTSTTSTCLPP  
 TNLPLGTVALPVTPVVTTPGQVSTPVSTTTSGVKPGTAPSKPPLTKAPVLPVGTLPAGTL  
 PSEQLPFPFGPSLTQSQQPLEDLDAQLRRTLSPEMITVTSAVGPVSMAPTAITEAGTQP  
 QKGVSVQKEGPVLATSSGAGVFKMGRFQVSVAADGAQKEGKNKSEDAKSVHFESSTSESS  
 VLSSSSPESTLVKPEPNGITIPGISSDVPESAHTTASEAKSDTGQPTKVGRFQVTTTAN  
 KVGRFSVSKTEDKITDTKKEGPVASPPFMDLEQAVLPAVIPPKEKPELSEPSHLNGPSSD  
 PEAAFLSRDVEDDGSGLSPHSPHQLSSKSLPSQNLSSQSLSNSFNSSYMSDNESEDI EDEDLK  
 LELRRLRDKHLKEIQDLQSRQKHEIESLYTKLGKVPPAVIIPPAAPLSGRRRRRPTKSKGS  
 KSSRSSSLGNKSPQLSGNLSGQSAASVLHPQQTLLHPPGNIPESGQNQLLQPLKPSPSDN  
 LYSFTSDGAISVPSLSAPGQGNKATIIIVQKQ

SEQ ID NO: 184\_BCON3\_H

MSEGESQTVLSSGSDPKVESSSSAPGLTSVSPVVTSTTSAASPEEEEESEDESEILEESP  
 CGRWQKRREEVNQRNVPGIDSAYLAMDTTEEGVEVWNEVQFSEKKNYKLQEEKVRAVFDN  
 LIQLEHLNIVKFHKEYWADIKENKARVIFITEYMSSGSLKQFLKKTCKNHKTMNEKAWKRW  
 CTQILSALSYLHSCDPPIIHGNLTCDTIFIQHNGLIKIGSVAPDTINNHHVKTCCREEQKNL  
 HFFAPEYGEVTNVTTAVDIYSFGMCALEMAVLEIQNGGESSYVPQEAISSAIQLLEDPLQ  
 REFIQKCLQSEPARRPTARELLFHPALFEVPSLKLLAAHCIVGHQHMI PENALEEITKNM  
 DTSAVLAEIPAGPGREPVTLYSQSPALEDKFLLEDVRNGIYPLTAFGLPRPQQPQQEEV  
 TSPVVPPSVKTPPTPEPAEVETRKVVLMQCNIESVEEGVKHHLTLLLKLEDKLNRLHSCDL  
 MPNENIPELAAELVQLGFI SEADQSRLTSLLEETLNKFNFNARNSTLN SAAVTVSS

SEQ ID NO: 185\_AA711829\_M

LKQFLKKTCKNHKTMNEKAWKRWCTQILSALSYLHSCDPPIIHGNLTCDTIFIQHNGLIK  
 IGSVAPDTINNHHVKTCCREEQKNLHFFAPEYGEVTNVTTAVDIYSFGMCALEMAVLEIQGN  
 GESSYVPQEAISSAIQLLEDLSLQREFIQKCLQSEPARRPTARELLFHPALFEVPSLKLLA  
 AHCIVGHQHMI PENALEEITKNMDTSAVLAEIPAGPGREPVTLYSQSPALEDKFLLEDV  
 RNGIYPLTAFGLPRPQQPQQEEVTSPVVPPSVKTPPTPEPAEVETRKVVLMQCNIESVEEG  
 VKHHLTLLLKLEDKLNRLHSCDLMPNESIPDLAAELVQLGFI SEADQSRLTSLLEETLNK  
 FNFTRNSTLNTATVTVSS

SEQ ID NO: 186\_AA099102\_H

MSSCVSSQPSSNRAAPQDELGGRGSSSSSESQKPCEALRGLSSLSIHLGMESFIVVTECEP  
 GCAVDLGLARDRPLEADGOEVPLDTSGSQARPHLSGRKLSLQERSQGGLAAGGSLDMNGR  
 CICPSLPYSPVSSPQSSPRLPRRPTVESHHVSITGMQDCVQLNQYTLKDEIGKGSYGVVK  
 LAYNENDNTYYAMKVLSKKKLIRQAAFPRRPPPRGTRPAPGGCIQPRGPIEQVYQEIAIL  
 KKLDHPNVVKLVLEVLD DPNEHDHLYMV FELVNQGPVMEVPTLKPLSEDQARFYFQDLIKGI  
 EYLHYQKIIHRDIKPSNLLVGEDGHIKIADFGVSNEFKGSDALLSNYVGTPAFMAPESLS  
 ETRKIFSGKAKDVWAMGVTLTYCFVFGQCPFMDERIMCLHSKIKSQALEFPDQPDIAEDLK  
 DLITRMLDKNPESRIVPEIKLHPWVTRHGAEPLPSEDENCTLVEVTEEEVENSVKHIPS  
 LATVILVKTMIRKRSFGNPFEGSRREERSLSAPGNLLTKKPTRECESLSELKEARQRRQP  
 PGHRPAPRGGGGSALVRGSPCVESCWAPAPGSPARMHPLRPEEAMEPE

SEQ ID NO: 187\_5R69\_17\_2\_H

MQEIPQEIQIKEIKKEQLSGSPWILLRENEVSTLYKGEYHRAPVAIKVFKKLQAGSIAIVR  
 QTFNKEIKTMKKFESPNILRIFGICIDETVTPPQFSIVMEYCELGTLLRELLDREKDLTLG

## FIGURE 1Q

KRMVLVLGAARGLYRLHHSEAPELHGKIRSSNFLVTQGYQVKLAGFELRKTQTSMSLGT  
REKTDREVKSTAYLSPQELEDVFYQYDVKSEIYSFGIVLWEIATGDI PFQGEEDWLSQW  
L

SEQ ID NO: 188\_H85811\_H  
MAPVYEGMASHVQVFSPTHLOSSAFCSVKKLKIEPSSNWDMTGYGSHSKVYSQSKNIPLS  
QPATTTVSTSLPVPNPSPLEQTI VFPSTGHI VVTSASSTSVTGQVLGGPHNLMRRSTV  
SLLDYQKCGLRKSEEIENTSSVQII EEHPPMIQNNASGATVATATTSTATSKNSGSNS  
EGDYQLVQHEVLCSMTNTYEVLFLGRGTFGQVVKCWKRGTEIVAIKILKNHPSYARQG  
QIEVSILARLSTESADDYNFVRAYECFQHKHNTCLVFEMLEONLYDFLKQNKFSPLPLKY  
IRPVLQQVATALMKLKSGLIHADLKPENIMLVDPSPRQPYRVKVIDFGSASHVSKAVCST  
YLQSRYYRAPEIILGLPFCEAIDMWSLGCVIAELFLGWPLYPGDSEYDQIRYISQTQGLP  
AEYLLSAGTKTTRFFNRDTSPLYPLWRLKTPDDHEAETGIKSKEARKYIFNCLDDMAQVN  
MTDLEGSMDLVEKADRREFIDLLKKMLTIDADKRITPIETLNHPFVTMTHLLDFPHSTH  
VKSCFQNMIEICKRRVNMVDTVNSKTPFITHVAPSTSTNLTMTFNNQLTTVHNQPSAASM  
AAVAQRSMPLOTGTAQICARPDPFQQAALIVCPPGFQGLQASPSKHAGYSVRMENAVPIVT  
QAPGAQPLQIQPGLLAQQA WPSGTQQILLPPAWQQLTG VATHTSVQHATVI PETMAGTQQ  
LADWRNTHAHGSHYNPIMQQPALLTGHVTLPAQA PLNVGVAVHVMRQQPTSTTSSRKSKQH  
QSSVRNVSTCEVSSSQAISSPQRSKRKENTPPRCAMVHSSPACSTSVTCGWGDVASSTT  
RERQRQTIVIPDTPSPTVSVITISSDTDEEEEQKHAPTSTVSKQRKNVISCVTVHDSPTS  
DSSSNTSPYSVQQRAGHNNANAFDTKGSLENHCTGNPRTIIVPPLKTQASEVLVECDLSV  
PVNTSHHSSSYKSKSSSNVTSTSGHSSGSSSGAITRQQRPGPHFQQQQPLNLSQAQQHI  
TTDRTGSHRRQQAYITPTMAQAPYSFPHNSPSHGTVHPLAAAAAAHLPTQPHLYTYTA  
PAALGSTGTVAHLVASQGSARHTVQHTAYPASIVHQVPVSMGPRVLPSPTIHPSQYPAQF  
AHQTYISASPASTVYTGYP LSPAKVNQYPYI

SEQ ID NO: 189\_DYRK3\_H  
MMIDETKCPPCSNVLCNPSEP PPPRRRLNMTAEQFTGDHTQHFLDGGEMKVEQLFQEFGNR  
KSNTIQSDGISDSEKCSPTVSQ GKSSDCLNTVKSNSSSSKAPKVVPLTPEQALKQYKHHLT  
AYEKL EII NYPEIYFVGPN AKKRHGVIGGPNNGGYDDADGAYIHVPRDHLAYRYEVLKII  
GKGSFGQVARVYDHKL RQYVALKMVRNEKRFHRQA AEEIRILEHLKKQDKTGSMNVIHML  
ESFTFRNHVCMAFELLSIDLYELIKKNKFQGF SVQLVRKFAQSILQSLDALHKNKIIHCD  
LKPENILLKHHGRSSTKVIDFGSSCFEYQKLYTYIQSRFYRAPEIILGSRYSTPIDIWSF  
RCILAEELLTGQPLFPGEDEGDQLACMMELLGMPPPKLLEQSKRAKYFIN SKGIPRYCSVT  
TQADGRVVLVGGRSRRGKKRGPPGSKDWGTALKGCDDYLFIEFLKRCLHWDPSARLTPAQ  
ALRHPWISKSVPRPLTTIDKVSGKRVVNPASAFQGLGSKLPPVVG IANKLKANLMSETNG  
SIPLCSVLPKLIS

SEQ ID NO: 190\_AA589241\_M DYRK3\_M  
TRPELLGMPPQKLLEQSKRAKYFIN SKGLPRYCSVSTQTDGRVVLLGGRSRRGKKRGPPG  
SKDWATALKGCGDYLFIEFLKRCLQWDPSARLTPAQALRHPWISKSTPKPLTMDKVPGKR  
VVNPTNAFQGLGSKLPPVVG IASKLKANLMSETSGSIPLCSVLPKLIS

SEQ ID NO: 191\_5R72\_16\_2\_H  
MAGGRGAPGRGRDEPPESYPQRQDHELQALEAIYGADFQDLRPDACGPVKEPPEINLVLY  
PQGLTGEEVYVKVDLRVKCPPTYPDVVPEIELKNAKGLSNESVNLLKSRLEELAKKHCGE  
VMIFELAYHVQSFLSEHNKPPPKSFHEEMLERRAQEEQQRLLLEAKRKEEQEQREILHEIQ  
RRKEEIKEEKKRKEMAKQERLEIASLSNQDHTSKKDPGGHRTAAI LHGGSPDFVGNKGHE  
ANSSGRSRRERQYSVCNSEDSPGSCEILYFNMGSPDQLMVHKGKCI GSDEQLGKLVYNAL  
ETATGGFVLLYEWVLQWQKKMGPF LTSSQEKEKIDKCKKQIQGTETEFNSLVKLSHPNVVR

## FIGURE 1R

YLAMNLKEQDDSI VVDIILVEHISGVSLAAHLSHSGPI PVHQLRRYTAQLLSGLDYLHSNS  
 VVHKVLSASNVLVDAEGTVKITDYSISKRLADICKEDVFEQTRVRFSDNALPYKTGKKGD  
 VWRGLGLLLLSLSQGGQECGEYPVTIPSDLPADFQDFLKKCVCLDDKERWSPQQLLKHSFIN  
 PPKMPLVEQSPEDSGGQDYVETVIPSNNRLPSAAFFSETQRQFSRYFIEFEELQLLGKGA  
 FGAVIKVQNKLDGCCYAVKRIPINPASRQFRRIKGEVTLLSRLHHENIVRYNAWIERHE  
 RPAGPGTPPPDSGPLAKDDRAARGQPASDTDGLDSEVAAAAPPILSSSVIEWSTSGERSAS  
 ARFPATGPGSSDDEDDDEDEHGGVFSQSFLPASDSESDIIFDNEDENSKSQNQDEDCNEK  
 NGCHESEPSVTTEAVHYLYIQMEYCEKSTLRDTIDQGLYRDTVRLWRLFREILDGLAYIH  
 EKGMIHRDLKPVNIFLDSDDHVKIGDFGLATDHLAFSADSKQDDQTGDLIKSDPSGHLTG  
 MVGTALYVSPEVQGSTKSAYNQKVDLFSLGIIFFEMSYHPMVTASERIFVLNQLRDPTSP  
 KFPEDFDDGEHAKQKSVISWLLNHDPKRPTATELLKSELLPPPQMEESESELHEVLHHTLT  
 NVDGKAYRTMMAQIFSQRISPAIDYTYDSDILKGNFSIRTAKMQQHVCETIIRIFKRHGA  
 VQLCTPLLLPRNRQIYEHNEAALFMDHSGMLVMLPFDLRIPFARYVARNNILNLKRYCIE  
 RVFRPRKLDRFHPKELLECAFDIVTSTTNSFLPTAEIITYIYEIIQEFPALQERNYSIYL  
 NHTMLLKAILLHCGIPEDKLSQVYIILYDAVTEKLTRREVEAKFCNLSLSSNSLCRLYKF  
 IEQKGDLDQDLMPTINSLIKQKTGIAQLVKYGLKDLEEVVGLLKKLGIKLQVLINLGLVYK  
 VQQHNGIIFQFVAFIKRRQRAVPEILAAGGRYDLLIPQFRGPQALGPVPTAIGVSIKIDK  
 ISAAVLNMEESVTISSCDLLVSVVGQMSMSRAINLTQKLWTAGITAEIMYDWSQSQEELQ  
 EYCRHHEITYVALVSDKEGSHVKVKSFEKERQTEKRVLETTELVDHVLQKLRTKVTDERN  
 REASDNLAVQNLKGSFSNASGLFEIHGATVVPISVLAPEKLSASTRRRYETQVQTRLQT  
 SLANLHQKSSEIEILAVDLPKETILQFLSLEWDADEQAFNTTVKQLLSRLPKQRYLKLVC  
 DEIYNIKVEKKVSVLFLYSYRDDYRILF

SEQ ID NO: 192\_R43524\_H, HRI\_H  
 MLGGNSGVRKREEEGDGAGAVAAPPAIDFPAEGPDPEYDESDVPAEIQVLKEPLQQPTFP  
 FAVANQLLLVSLLLEHLSHVHEPNPLRSRQVFKLLCQTFIKMGLLSSFTCSDEFSSRLHH  
 NRAITHLMRSAKERVQRDPCEDISRIQKIRSREVALEAQTSRYLNEFEELVILGKGGYGR  
 VYKVRNKLDGQYYAIKKILIKGATKTVCMKVLREVKVLAGLQHPNIVGYHTAWIEHVHVI  
 QPRADRAAIELPSLEVLSHQEEDREQCGVKNDSSSSSIIFAEPTPEKEKRFGESDTENQ  
 NNKSVKYTTNLVIRESGELESTLELQENGLAGLSASSIVEQQPLLRNSHLEESFTSTEE  
 SSEENVNFLGQTEAQYHMLLHIQMQLCELSLWDWIVERNKRGREYVDESACPYVMANVAT  
 KIFQELVEGVFYIHNMGIVHRDLKPRNIFLHGPDQQVKIGDFGLACTDILQKNTDWTNRN  
 GKRTPTHTSRVGTCLYASPEQLEGSEYDAKSDMYSLGVVLELQFPFGTEMERAEVLTGL  
 RTGQLPESLRKRCVPVQAKYIQHLTRNSSQRPSAIQLLQSELFQNSGNVNLTLMKII EQ  
 EKEIAELKKQLNLLSQDKGVRDDGKDGGVG

SEQ ID NO: 193\_17000057519457\_H  
 MAAARATTPADGEEPAPAEALAAARERSRFLSGLELVKQGAEARVFRGRFQGRAAVIK  
 HRFPGKYRHPALEARLGRRRTVQEARALLRCRRAGISAPVVFFVDYASNCLYMEEIEGSV  
 TVRDYIQSTMETEKTPQGLSNLAKTIGQVLARMHDEDLIHGDLTTSNMLLKPPLEQLNIV  
 LIDFGLSFISALPEDKGVDLYVLEKAFLSTHPNTETVFEAFLKSYSTSSKKARPVLKKLD  
 EVRLRGRKRSMVG

SEQ ID NO: 194\_AA013524\_M  
 LVQQGAEARVFRGRFQGRAAVVKHFRPKSYRHPELEARLGRRRTVQEARALLRCRRAGIA  
 APVVFFVDYASNCLYMEEIEDSVTVRDYIQSTMETEKDPQCLLDLARRMGQVLAGMHDQD  
 LIHGDLTTSNMLLRPLAQLHIVLIDFGLSFVSGLPEDKGVDLYVLEKAFLSTHPHTETA  
 FEAFLKSYGASSKKSSPVLKKLDEVRLRGRKRSMVG



## FIGURE 1S

SEQ ID NO: 195\_17000139801197\_H, IRAKM\_H  
MAGNCGARGALSAHTLLFDLPPALLGELCAVLDS CDGALGWRGLAERLSSSWLDVRHIEK  
YVDQKGSGTRELLWSWAQKNKTIGDLLQVLQEMGHRRRAIHLITNYGAVLSPSEKSYQEGG  
FPNILFKETANVTVDNVLIPHENEKGVLLKSSISFQNIIEGTRNFHKDFLIGEGEIFEVY  
RVEIQNLTYAVKLFKQEKMKQCKKHWKRFLSELEVLLLFHHPNILELAAYFTETEFCL  
YPYMRNGTLFDRLQCVGDTAPLPWHIRIGILIGISKAIHYLHNVQPCSVICGSISSANIL  
LDDQFQPKLTDFAMAHFRSHLEHQSTINMTSSSSKHLWYMPEEYIRQGKLSIKTDVYSF  
GIVIMEVLTGCRVVLDDPKHIQLRDLLRELMKRGDLSCLSLDKKVPKPCPRNFSKLF  
LAGRCAATRALKRPSMDEVLTLESTQASLYFAEDPPTSLKSFRCPSPLFLENVPSIPVE  
DDESQNNNLLPSDEGLRIDRMTQKTPFECSQSEVMFLSLDKKPKESKRNEEACNMPSSSCE  
ESWFPKYIVPSQDLRPYKVNIDPSSEAPGHSCRSRPVESSCSSKFSWDEYEYQYKKE

SEQ ID NO: 196\_AA840598\_M IRAKM\_M  
MWKRFLSELEVLLLFRRHPHILELAAYFTETEFCLVYPYMSNGTLFDRLQCTNGTTPLSW  
HVRISVLIGIAKAIQYLHNTQPCAVICGNVSSANILLDDQQLPKLTDFAAAHFRPNLEQQ  
SSTINMTGGGRKHLWYMPEEYIRQGRLSVKTDVYSFGIVIMEVLTGCKVVLDDPKHVQLR  
DLLMELMEKRGDLSCLSLDRKI PPCPRNFSKLFSLAGRCVATKAKLRPTMDEVLSLE  
STQPSLYFAEDPPTSLKSFRCPSPLFLDNVPSIPVEDDENQNNHSPVPKEVLGTDRTVQK  
TPFECSQSEVTFLGLDRNRGNRGSEADCNPSSSHEECWSPELVAPSQDLSPTVISLGSS  
WEVPGHSYGSKPKMEKRCSSGLFCSEHEQSKKQ

SEQ ID NO: 197\_AA088547\_H  
MASAVRGSRPWPRLGLQLQFAALLGLTSPQVHTLRPENLLLVSTLDGSLHALSKQTGDL  
KWTLRDDPVIIEGPMYVTEMAFLSDPADGSLYILGTQKQGLMKLPFTIPELVHASPCRSS  
DGVFYTGKQDAWFVVDPESETQMTLTTEGPSTPRLYIGRTQYTVTMHDPRAPALRWNT  
TYRRYSAPPMDGSPGKYMSHLASC GMGLLLTVDPGSGTVLWTQDLGVPVMGVYTWHDGL  
RQLPHLT LARDTLHFLALRWGHIRLPASGPRDTATLFTLDTQLLMTLYVGKDETGFYVS  
KALVHTGVALVPRGLTLAPADGPTTDEVTLQVSGEREGSPSTAVRYPSSGVALPSQWLLI  
GHHELPPVLHTTMLRVHPTLGSGTAETRPPENTQAPAFFLELLSLSREKLWDSELHPEEK  
TPDSYLGLGPQDLLAASLTAVLLGGWILFVMRQVVEKQQETPLAPADFAHISQDAQSLHS  
GASRRSQKRLQSPSKQAQPLDDPEAEQLTVVGKISFNPKDVLGRGAGGTFFVFRGQFEGRA  
VAVKRLRECFGLVRREVQLLOESDRHPNVLRYFCTERGPQFHYIALELCRASLQEYVEN  
PDLDRGGLEPEVVLQQLMSGLAHLHSLHIVHRDLKPGNILITGPDSQGLGRVVLSDFGLC  
KKLPAGRCFSLSHSGIPGTEGWMAPELLQLLPDSPTS AVDI FSAGCVFYVLSGGSHPF  
GDSLYRQANILTGAPCLAHLEEEVHDKVVARDLVGAMLSPLPQPRPSAPQVLAHPFFWSR  
AKQLQFFQDVSDWLEKESEQEPLVRALEAGGCAVVRDNWHEHIS MPLQTDLRKFRSYKGT  
SVRDLLRAVRNKKHHYREL PVEVRQALGQVPDGFVQYFTNRFPRLLLHTHRAMRSCASES  
LFLPYYPDPSEARRPCPGATGR

SEQ ID NO: 198\_HGP\_6644466  
MEGISNFKTPSKLSEKKKSVLCSTPTINIPASPFMQKLGFGTGVNVYLMKRS PRGLSHSP  
WAVKKINPICNDHYRSVYQKRLMDEAKILKSLHHPNIVGYRAFTEANDGSLCLAMEYGGG  
KSLNDLIEERYKASQDPFPAAIILKVALNMARGLKYLHQEKLLHGD IKSSNVVIKGD FE  
TIKICDVGVSLPLDENMTVTDPEACYIGTEPWKPKEAVEENGVI TDKADIFAFGLTLWEM  
MTLSIPHINLSNDDDDDEDKTFDESDFDDEAYYAALGTRPPINMEELDESYQKVIELFSVC  
TNEDPKDRPSAAHIVEALETDV

SEQ ID NO: 199\_AA449542\_M  
SPRGLSHSPWAVKKISLLCDDHYRTVYQKRLTDEAKILKNLNHPNII GYRAFTEASDGSL  
CLAMEYGGGEKSLNDLIEERNKDSGSPFPAAVILRVALHMARGLKYLHQEKLLHGD IKSS



## FIGURE 1T

NVVIKGFETIKICDVGVSLPLDENMTVTDPEACYIGTEPWKPKEALEENGIITDKADV  
AFGLTLWEMMTLCIPHVNLPDDDDVDEDATFDESDFDDEAYYAALGTRPSINMELDDSYQK  
AIELFCVCTNEDPKDRPSAAHIVEALELDGQCCGLSESKH

SEQ ID NO: 200\_5R57\_10\_2\_M TESK2\_M  
LLDSDLYLPWTVRVKLAYGIAVGLSYLHFKGIFHRDLTSKV

SEQ ID NO: 201\_AA232253\_H  
MSSLGASFVQIKFDDLQFFENC GGSGSVYRAKWI SQDKEVAVKKLLKIEKEAEILSVL  
SHRNIIQFYGVILEPPNYGIVTEYASLGSLYDYINSNRSEEMDMDHIMTWATDVAKGMHY  
LHMEAPVKVIHRDLKSRNVVIAADGV LKICDFGASRFHNHTTHMSLVGTFPWMAPEVIQS  
LPVSETCDTYSYGVVLWEMLTREV PFKGLEGLQVAWLVEKNERLTIPSSCPRSFAELLH  
QCWEADAKKRPSFKQII SILESMSNDTSLPDKCNSFLHNKAEWRCIEATLERLKKLERD  
LSFKEQELKERERR LKMWEQKLTEQSNTPLLPSFEIGAWTEDDVYCWVQQQLVRKGDSSAE  
MSVYASL FKENNITGKRLLLLLEEEDLKDMGIVSKGHI IHFKSAIEKLTHDYINLFHFPPL  
IKDSGGPEEENEKIVNLELVFGFHLKPGTGPQDCKWKMYMEMDGDEIAITYIKDVTFNT  
NLPDAEILKMTKPPFVMEKWIVGIAKSQTVECTVTYESDVRTPKSTKHVHLIQWSRTKPQ  
DEVKAVQLAIQTLFTNSDGNPGSRSDSSADCQWLDTLRMROIASNTSLQRSQSNPILGSP  
FFSHFDGQDSYAAAVRRPQVPIKYQQITPVNQSRSSSPTQYGLTKNFSSLHLNSRDSGFS  
SGNTDTSSERGRYSDRSRNKYGRGSI SLNSSPRGRYSGKSQHSTPSRGRYPGKFYRVSQS  
ALNPHQSPDFKRSPRDLHQPN TIPGMPLHPETDSRASEEDSKVSEGGWTKVEYRKKPHRP  
SPAKTNKERARGDHRGWRNF

SEQ ID NO: 202\_AI375137\_H  
MGNYKSRPTQTCTDEWKKKVSESYVITIERLEDDLQIKEKELTEL RNIFGSDEAFSKVNL  
NYRTENGLSLLHLCCICGGKKSHIRTLMLKGLRPSRLTRNGFTALHLAVYKDNAELITSL  
LHSGADIQQVGYGGLTALHIATIAGHLEAADVLLQHGANVNIQDAVFFTPLHIAAYYGHE  
QVTRLLLKFGADV NVSGEVGDRPLHLASAKGFLNIAKLLMEEGSKADVNAQDNEDHVPLH  
FCSRFGHHDIVKYLLQSDLEVQPHVNIYGDTPHLACYN GKFEVAKEIIQISGTESLTK  
ENIFSETAFHSACTYGKSIDL VKFLLDQNVININHQGRDGHTGLHSACYHGHIRLVQFLL  
DNGADMNLVACDPSRSSGEKDEQTCLMWAYEKGHD AIVTLLKHYKRPQDELPCNEYSQPG  
GDGSYVSVPSPLGKIKSMTKEKADILLRAGLPSHFHLQLSEIEFHEIIGSGSFGKVYKG  
RCRNKIVAIKRYRANTYCSKSDVDMFCREVSILCQLNHPCV IQFVGACLN DPSQFAIVTQ  
YISGGSLSLLEHQKRILD LQSKLIIAVDVAKGMEYLHNLTQPIIHRDLNSHNILLYEDG  
HAVVADFGESRFLQSLDEDNMTKQPGNLRWMAPEVFTQCTRYTIKADVFSYALCLWEILT  
GEIPFAHLKPAAAAAD MAYHHIRPPIGYSIPKPISSLLIRGWNACPEGRPEFSEVVMKLE  
ECLCNIELMSPASSNSSGSLSPSSSSDCLVNRGGPGRSHVAALRSRFELEYALNARSYAA  
LSQSAGQYSSQGLSLEEMKRS LQYTPIDKYGYVSDPMSSMHFHS CRNSSSFEDSS

SEQ ID NO: 203\_H97685\_H  
MESERSPLYRQLIDLGYLSSSHWNC GAPGQDTKAQSMLVEQSEKLRHLSTF SHQVLQTRL  
VDAAKALNLVHCHCLDI FINQAFDMQRDLQITPKRLEYTRKKENELYESLMN IANRKQEE  
MKDMIVETLNTMKEELLDDATNMEFKDVIVPENGE PVGTREIKCCIRQIQELIISRLNQA  
VANKLISSVDYLRESFVGTLERCLQSLEKSQDVSVHITSNYLKQILNAA YHVEVTFHSGS  
SVTRMLWEQIKQIIQRITWVSPPAITLEWK RKVAQEAIESLSASKLAKSICSQFRTRLNS  
SHEAFAASLRQLEAGHSGRLEKTEDLWLRVRKD HAPRLARLSLESRLQDVLLHRKPKLG  
QELGRGQYGVVYLCDNWGGHFPCALKSVVPPDEKHWNDL ALEFHYMRSLPKHERLVDLHG  
SVIDYNYGGGSSIAVLLIMERLHRDLYTGLKAGLTLETRLQIALDVVEGIRFLHSQGLVH  
RDIKLNVL LDKQNRAKITDLGFCKPEAMMSGSIVGTPIHMAPELFTGKYDNSVDVYAFG

## FIGURE 1U

ILFWYICSGSVKLPEAFERCASKDHLWNNVRRGARPERLPVFDEECWQLMEACWDGDPLK  
RPLLGI VQPM LQGIMNRLCKSNSEQPNRGLDDST

SEQ ID NO: 204\_W20810\_M  
DVNLKASKASDVYSFGILVWAVLAGREAELVDKTS LI RETVCDRQSRPPLTELPPGSPET  
PGLEKLKELMIHCWGSQSENRP SFQDCEPKTNEVYNLVKDKVDAAVSEVKHYLSQHRSSG  
RNLSAREPSQRGTEMDCPRETMVSKMLDRLHLEEPSGPVPGKCPERQAQDTSVGPATPAR  
TSSDPVAGTPQIPHTLPFRGTTTPGPVFTETPGPHQPNQGDGRHGTPWYPWTPPNPMTGP  
PALVFNNCSEVQIGNYNLSLVAPPRTTASSSAKYDQAQFGRGRGWQPFHK

SEQ ID NO: 205\_AA744236\_H  
MGSENSALKSYTLREPPFTLPSGLAVYPAVLQDGKFASVFVYKRENEDKVNKA AKHLKTL  
RHPCLLRFLSCTVEADGIHLVTERVQPLEVALETLSAEVCAGIYDILLALIFLHDRGHL  
THNNVCLSSVFVSEDGHWKLGGMETVCKVSQATPEFLRSIQSIRDPASIPPEEMSPEFTT  
LPECHGHARDAFSFGTLVESLLTILNEQVSADVLSSFQOTLHSTLLNPIPKCRPALCTLL  
SHDFFRND FLEVVNFLKSLTLKSEEEKTEFFKFLLD RVSCLSEELIASRLVPLLLNQLVF  
AEPVAVKSFLPYLLGPKKDHAQGETPCLLSPALFQSRVIPVLLQLFEVHEEHVRMVLLSH  
IEAYVEHFTQEQLKKVILPQVLLGLRDTSDSIVAITLHSLAVLVSLLGPEVVVGERTKI  
FKRTAPSFTKNTDLSLEGDPFSQPIKFPINGLSDVKNTSEDS ENFPSSSKKSEEPDWSE  
PEEPENQTVNIQIWPREPCDDVKSQCTTLDVEESSWDDCEPSSLDTKVNPGGGITATKPV  
TSGEQKPIPALLSLTEESMPWKSSLPQKISLVQRGDDADQIEPPKVSSQERPLKVPSELG  
LGEEFTIQVKKKPKVDPEMDWFADMIPEIKPSAAFLILPELRTEMVPPKDDVSPVMQFSS  
KFAAAEITEGEAEGWEEEGELNWEDNNW

SEQ ID NO: 206\_AI052250\_H  
MESMLNKLKSTVTKVTADVTSAVMGIPVTREFDVGRHIASGCNGLAWKIFNGTKKSTKQE  
VAVFVFDKKLIDKYQKFEKDQIIDSLKRGVQQLTRLRHPRLLT VQHPLEESRDCLAFCTE  
PVFASLANVLGNWENLPSPISPDIKDYKLYDVETKYGLLQVSEGLSFLHSSVKMVHGNIT  
PENIILNKSGAWKIMGFDFCVSSTNPSEQEPKFPCKEWDPNLP SLCLPNPEYLAPEYILS  
VSCETASDMYSLGTVMYAVFNKGKPIFEVNKQDIYKSFSRQLDQLSRLGSSSLTNIPEEV  
REHVKLLLNVTPTVRPDADQMTKIPFFDDVGAVTLQYFDTLFQ RDNLQKSQFFKGLPKVL  
PKLPKRIVIVQRILPCLTSEFVNPDMPFVLPNVLLIAEECTKEEYVKLILPELGPVFKQQ  
EPIQILLIFLQKMDLLLT KTTPDEIKNSVLPMVYRALEAPSIQIQELCLNI IPTFANLID  
YPSMKNALIPRIKNACYKHLPLRFV

SEQ ID NO: 207\_AA278842\_H  
MWFFARDPVRDFPFELIPEPPEGGLPGPWALHRGRKKATGSPVSI FVYDVKPGAEEQTQV  
AKAAFKRFKTLRHPNILAYIDGLETEKCLHVVT EAVTPLGIYLKARVEAGGLKELEISWG  
LHQIVKALSFLVNDCSLIHNNVCMAAVFVDRAGEWKLGGLDYMYS AQGNNGGGPPRKGIP E  
LEQYDPPELADSSGRVVREKWSADMWRLGCLIWEVFNGPLPRAAALRNPGKIPKTLVPHY  
CELVGANPKVRPNPARFLQNCRAPGGFMSNRFVETNLFLEEIQIKEPAEKQKFFQELSKS  
LDAFPEDFCRHKVLPQLLTAFEFGNAGAVVLTPLFKVGKFLSAEEYQQKIIPVVVKMFSS  
TDRAMRIRLLQQMEQFIQYLDEPTVNTQIFPHVHGF LDTNPAIREQTVKSMLLLAPKLN  
EANLNVELMKHFARLQAKDEQGPIRCNTTVCLGKIGSYLSASTRHRVLTSAFSRATRDPF  
APSRVAGVLGFAATHNLYSMNDCAQKILPVLCGLTVDPEKSVRDQAFKAIRSFLSKLESV  
SEDPTQLEEVEKDVAHAASSPGMGGAASWAGWAVTGVSSLT SKLIRSHPTTAPTETNIPQ  
RPTPEGVPAPAPTVPATPTTSGHWETQEEDKDTAEDSSTADRWDDEDWGSLEQEAESVL  
AQQDDWSTGGQVSRASQVSNSDHKSSKSPESDWSSWEAEGSWEQGWQEPSSQEP PPDGTR  
LASEYNWGGPESSDKGDPFATLSARPSTQPRPDSWGEDNWEGL ETDSRQVKAELARKKRE  
ERRREMEAKRAERKVAKGPMKLGARKLD

## FIGURE 1V

SEQ ID NO: 208\_AA599286\_H

MAFMEKPPAGKVLLDDTVPLTAAIEASQSLQSHTEYIIRVQGGISVENSWQIVRRYSDFD  
LLNNSLQIAGLSLPLPPKKLIGNMDREFIAERQKGLQNYLNVITTNHILSNCELVKKFLD  
PNNYSANYTEIALQQVSMFFRSEPKWEVVEPLKDIGWRIRKKYFLMKIKNQPKERLVLSW  
ADLGPDKYLSDKDFQCLIKLLPSCLHPYIYRVTFATANESSALLIRMFNEKGTLDLIYK  
AKPKDPFLKKYCNPKKIQGLELQQIKTYGRQILEVLKFLHDKGFPYGHLHASNVMLDGD  
CRLDLENSLLGLPSFYRSYFSQFRKINTLESVDVHCFGHLLYEMTYGRPPDSVPVDSFP  
PAPSMVAVVLESTLSCEACKNGMPTISRLLOMPLFSDVLLTTSEKPOFKIPTKLKEALR  
IAKECIEKRLIEEQKQIHQHRRLTRAQSHHGSEEERKKRKILARKKSKRSALENSEEHS  
KYSNSNNSAGSGASSPLTSPSSPTPPSTSGISALPPPPPPPPPPAAPLPPASTEAPAQLS  
SQAVNGMSRGALLSSIQNFQKGTLRKAKPVITVLRRSAEASCLHLEGKVLFYSSPLPPN  
YPLPGKVIAEPVQPQTVLFCRCSCCKQLFERNNSLSRIKLGWHAKKKKKK

SEQ ID NO: 209\_AA425725\_H

MSASTGGGGDSGGSGGSSSSSQASCGPESSGSELALATPVPQMLQGLLGSDDEEQEDPKD  
YCKGGYHPVKIGDVFNGRYHVVRKLGWGHFSTVWLCWDIQRKRFVALKVVKSAAGHYTETA  
VDEIKLLKCVRDSDPSDPKRETIQVLIIDFRISGVNGVHVCMLVLEVLGHQLLKWI IKS  
NYQGLPVPVCVKSIVRQVLHGLDYLTHTCKIIHTDIKPENILLCVGDAYIRRLAAEATEWQQA  
GAPPPSRISIVSTAPQEVLTGKLSKNKRKKMRRKRKQOKRLLEERLRDLQRLEAMEAATQA  
EDSGLRLDGGSGSTSSSGFSGSLFSPASCSILSGSSNQRETGGLLSPSTPFGASNLLVNP  
LEPQNADKIKIKIADLGNACWVHKHFTEDIQTRQYRAVEVLIGAEGPADIWSTACMAF  
ELATGDYLFEPHSGEDYSRDEDHIAHIVELLGDI PPAFALSGRYSREFFNRRGELRHIHN  
LKHWGLYEVLMEKYEWPLEQATQFSAFLLPMMEYIPEKRASAADCLQHPWLNP

SEQ ID NO: 210\_SGK022\_H

MEDFLLSNGYQLGKTIGEGTYSKVKEAFSKKHQRKVAIKVIDKMGGPSEFIQRFLPRELQ  
IVRTL DHKNIIQVYEMLESADGKICLVMELAEGGDVFD CVLNGGPLPESRAKALFRQMVE  
AIRYCHGCGVAHRDLKCENALLQGFNLKLTDFGFAKVLPKSHRELSQTFCGSTAYAAPEV  
LQGI PHDSKKGDVWSMGVVLYVMLCASLPFDDTDI PKMLWQQQKGVSFPTHLSISADCQD  
LLKRLLEPDMILRPSIEEVSWHPWLAST

SEQ ID NO: 211\_AA060026\_M SGK022\_M

MEDFLLSNGYQLGKTIGEGTYSKVKEAFSKKHQRKVAIKIIDKMGGPEEFIQRFLPRELQ  
IVRTL DHKNIIQVYEMLESADGKIYLVMELEAGGDVFD CVLNGGPLPESRAKALFRQMVE  
AIRYCHGCGVAHRDLKCENALLQGFNLKLTDFGFAKVLPKSRRELSQTFCGSTAYAAPEV  
LQGI PHDSKKGDVWSMGVVLYVMLCASLPFDDTDI PKMLWQQQKGVSFPTHLGISTECQD  
LLKRLLEPDMILRPSIEEVSWHPWLAST

SEQ ID NO: 212\_AA399669\_H

MGKGDVLEAAPT TTTAYHSLMDEYGYEVGKAIGHGSYGSVYEAFYTKQKVMVAVKII SKKK  
ASDDYLNKFLPREIQQVMKVLRHKYLINFYRAIESTSRVYIIILELAQGGDVLEWIQRYGA  
CSEPLAGKWFSQTLGLIAYLHKSIVHRDLKLENLLLDKWENVKISDFGFAKMVPSNQPV  
GCSPXYRQVNCFSHLSQTYCGSFAYACPEILRGLPYNPFLSDTWSMGVILYTLVVAHLPP  
DDTNLKKLLRETQKEVTFPANHTISQECKVQLLIACVAQWRKTQARPLSPLL

SEQ ID NO: 213\_AA758539\_H

MDDATVLRKKGYIVGINLGKGSYAKVKSAYSERLKFNVAVKIIDRRKTPTDFVERFLPRE  
MDILATVNHGSI IKTYEIFETSDGRIYIIMELGVQGDLLFEIKCQ GALHEDVARKMFRQL  
SSAVKYCHDLDIVHRDLKCENLLLDKDFNIKLSDFGFSKRCLRDSNGRIILSKTFCGSAA

## FIGURE 1W

YAAPEVLQSIPIYQPKVYDIWSLGVILYIMVCGSMPYDDSDIRKMLRIQKEHRVDFPRSKN  
LTCECKDLIYRMLQPDVSRQLHIDEILSHSWLQPPKPKATSSASFKEGEGKYRAECKLD  
TKTGLRPDHRPDHKLGAKTQHRLLVVPENENRMEDRLAETSRAKDHHISGAEVGKAST

SEQ ID NO: 214\_AA883975\_H

MSGDKLLSELGYKLGRTIGEGSYSKVKVATSKKYKGTVAIKVVDRRRAPPDFVNKFLPRE  
LSILRGVRHPHIVHVFEFIEVCNGKLYIVMEAAATDLLQAVQORNGRIPGVQARDLFAQIA  
GAVRYLHDHHLVHRDLKCENVLLSPDERRVKLTDFGFGGRQAAGYPDLSTTYCGSAAYASP  
EVLLGIPYDPKKYDVWSMGVVLYVMVTGCMFDDSDIAGLPRRQKRGVLYPEGLELSERC  
KALIAELLQFSPSARPSAGQVARNCWLRAGDSG

SEQ ID NO: 215\_AA905446\_H

VGRQETGVRRWAFILCQPI SPPLTSSEFIQRFLPRELQIVRTLDHKNIIQVYEMLESADG  
KICLVMELAEGGDVFDVLCVNGGGLPESRAKALFRQMVEAIRYCHGCGVAHRDLKCENALL  
QGFNLKLTDFGFAKVLPKSHRELSQTFCGSTAYAAPEVLQGI PXKMLWQQQKGVSFPTH  
SISADCQDLLKRLLEPDMILRPSIEEVSWHPWLAST

SEQ ID NO: 216\_H29974\_H

YSLLAIEIGRGSYGVVYEAVAGRSGARVAVKKIRCDAPENVELALAEFWALTSLKRRHQNV  
VQFEECVLQORNGLAQRMSHGKNSQLYLRLVETSLKGERILGYAEPCYLWFMVMEFCEGG  
DLNQYVLSRRPD PATNKSFMLQLTSAIAFLHKNHIVHRDLKPDNILITERSGTPILKVAD  
FGLSKVCAGLAPRGKEGNQDNKNVNVNKNYWLSSACGSDFYMAPEVWEGHYTAKADIFALG  
IIIWAMIERITFIDSETKKELLGTYIKQGTEIVPVGEALLENPKMELHIPQKRRTSMSEG  
IKQLLKDMMLAANPQDRPDAFELETRMDQVTCAA

SEQ ID NO: 217\_AA498104\_M H29974\_M

PLLLPPPPAAMETGKENGARRGTS PERKRRSPVQORVLCEKLRPAAQAMDPAGAEVPGEA  
FLARRRPDGGGGDV PARPRYSLLAEIGRGSYGVVYEAVAGRSGARVAVKKIRCDAPENVE  
LALAEFWALTSLKRRHQNI VQFEECVLQORNGLAQRMSHGKNSQLYLRLVETSLKGERIL  
GYAEPCYLWFMVMEYCEGGDLNQYVLSRRPD PATNKSFMLQLTSAIAFLHKNHIVHRDLK  
PDNILITERSGTPILKVAD FGLSKVCAGLAPRGKEGNQDNKNVNVNKNYWLSSACGSDFYM  
APEVWEGHYTAKADIFALGIIIWAMIERITFIDSETKKELLGTYIKQGTEIVPVGEALLE  
NPKMELHIPQKRRTSMSEGVKQLLKDMMLAANPQDRPDAFELETRMDQVTCAA

SEQ ID NO: 218\_AA215311\_H

MVSSQPKYDLIREVGRGSYGVVYEAVIRKTSARVAVKKIRCHAPENVELALREFWALSSI  
KSQHPNVIHLEECILQKDMVQKMSHGSSSLYLQLVETSLKGEIAFDPRSAYYLWFMVMD  
FCDGGDMNEYLLSRKPNRKTNTS FMLQLSSALAFHKNQIIHRDLKPDNILISQTRLDT  
DLEPTLKVADFGLSKVCSASGQNPEEPVSVNKCFLSTACGTDFYMAPEVWEGHYTAKADI  
FALGIIIWAMLERITFIDTETKKELLGSYVKQGTEIVPVGEALLENPKMELLI PVKKKSM  
NGRMKQLIKEMLAANPQDRPDAFELELRVLVQIAFKDSSWET

SEQ ID NO: 219\_AA018361\_H

MRAAFPAGGAGGSVEPPSARPAPQ PAGTAARSEEAPARAQAAGMAGPGWGPRLDGFILT  
ERLGS GTYATVYKAYAKKTREVVAIKCVAKKSLNKASVENLLTEIEILKGIRHPHIVQL  
KDFQWSDNIYLIMEFCAGGDL SRFIHTRRILPEKVARVFMQQLASALQFLHERNISHLD  
LKPQNILLSSLEKPHLKLADFGFAQHMSPWDEKHVLRGSPLYMAPEMVCQRQYDARVDLW  
SMGVILYEALFGQPPFASRSFSELEEKIRSNRVIELPLRPLLSRDCRDLLQRLLERDPSR  
RISFQDFFAHPWVDLEHMPSGESLGRATALVVQAVKKDQEGDSAAALS LYCKALDFFVPA



## FIGURE 1X

LHYEVDAQRKEAIKAKVGQYVSRAEELKAIVSSSNQALLRQGTSA RDLLREMARKPRLL  
AALEVASAAMAKEEAAGGEQD DALDYQHSLGELL LLLRS PRAGGGSCFTLRFR TSWPELN  
T

SEQ ID NO: 220\_AA311714\_H

MENFILYEEIGRGSKTVVYKGRRKGTINFVAILCTDKCRRPEITNWVRLTREIKHKNI VT  
FHEWYETSNHLWLVLXENLPEDVVREFGIDLISGLHHLHKLGLIFCDISPRKILLEGPGTL  
KFSNFCLAKVEGENLEEFFALVAAEEGGGDNGENVLKKSMKSRVKGSPVYTAP EVVRGAD  
FSISSDLWSLGC LLYEMFSGKPPFFSESVSELTEKILCEDPLPPIPKDSSRPKASSDFIN  
LLDGLLQRDPQKRLTWTRLLQHSFWKKAFAGADQESSVEDLSLSRNTMECSGPQDSKELL  
QNSQSRQAKGHKSGQPLGHSFRLENPTEFRPKSTLEGQLNESMFL LSSRPTPRTSTAVEV  
SPGEDMTHCSPQKTSPLTKITSGHLSQQDLESQMRELIYTDSDLVVTPIIDNP KIMKQPP  
VKFDAKILHLPTYSVDKLLFLKDQDWNDFLQQVCSQIDSTEKSMGASRAKLNLLCYLCVV  
AGHQEVATRLLHSPLFQLLIQHLRIAPNWDIRAKVAHVIGLLASHTTELQENTPVVETTS  
SIGIGILNCLVQHSTPVPRQCLVYV

SEQ ID NO: 221\_SGK384\_H

SLAHVLRARQILTEPEVRDYL RGLVSGLRYLHQRCILHR

SEQ ID NO: 222\_AA210451\_M SGK384\_M

MGQQHGTRNGLTHRELPRGVGLLLAMALMNVALYLCLDQLFISPGRSTADSRRCPPGYFR  
MGRMRNCSRWLSCEELRTEVRQLKRVGEGAVKRVFLSEWKEHKVALSRLTRLEMKEDFLH  
GLQMLKSLQSEHVVTLVGYCEEDGTILTEYHPLGSLSNLEETLNLSKYQDVNTWQHRLQL  
AMEYVSIINYLHHSPLGTRVMCDSDNDLPKTL SQYLLTSNFSIVANDLDALPLVDHDSGVL  
IKCGHRELHGDFVAPEQLWPYGEDTPFQDDLMP SYNEKVDIWKIPDVSSFLLGHVEGSDM  
VRFHLFDIHKACKSQIPAERPTAQNVLDAYQRVFHS LRDTVMSQTKEML

RM200000-5M0 (0000000000)

SEQ ID NO: 223\_SGK071\_2\_H

EVVAVQMMVECMDDHYASQALEELMPLLKLRHAHISVYQELFITWNGEISSLYLC LVMEF  
NELSFQEVIEDKRKAKKIIDSEWMQNVLGQVLD ALEYLHHLDI IHRNLKPSNIILISSDH  
CKLQDLSSNVLMTDKAKWNIRAEEDPFRKSWMAPEALNFSFSQKSDIWSLGCII LDMTSC  
SFMDGTEAMHLRKS LRQSPGSLKAVLKTMEEEKQIPDVETFRNLLPLMLQIDPSDRITIKD  
VVHITFLRGSFKSSCVSLTLHRQMVPASITDMLLEGNVASILGDAGDTKGERALKLLSMA  
LASYCLVPEGSLFMPLALLHMH DQWLS CDQDRVPGKRDFASLGKLGKLLGPIPKGLPWPP  
ELVEVVVTMELHDRVLDVQLCACSLLLHLLGQALVHHPEAKAPCNQAITSTLLSALQSH  
PEEEPLLVMVYSLLAITTTQES ELS EELQNAGLLEHILEHLNSSL ES RDVCASGLGLLW  
ALLLDDPILALQRPRKKRAPNHGKPGKPKNPASTQSIIVNKAPLEKVPDLISQVLATYPA  
DGEMAEASCGVFWLLSLLGCIKEQQFEQVALLLQSIRLCQDRALLVNNAYRGLASLVKV  
SELA AFKV VVQEEGGSGLSLIKETYQLHRDDPEVVENVGMLLVHLASYEEILPELVSSSM  
KALLQEIKERFTSSLVSDSSAFSKPGLPPGGSPQLGCTTSGGLE

SEQ ID NO: 224\_AA118352\_M SGK071\_M

EEDPCQKSWMAPEALKFSFSTKSDIWSLGCII LD MATCSFLNDTEAMQLRKAIRHHPGSL  
KPILKTMEEEKQIPGTDVYYLLLPFMLHINPSDR LAIKDVMQVTFMSNSFKSSSVALNMQR  
QKVPIFITDVLLLEGNMANILGSWLCASFVNDSRHCD SGIGSQRLGFDFQSVSWTEHPLKD  
VMQNFSSRPEVQLRAINKLLTMPEDQLGLPWPTELLEVISI IKQHGRILDILLSTCSLL  
LRVLGQALAKDPEAEIPRSSLIISFLMDTLRSHPN SERLVNVVYNVLAIISSQGQISEEL  
EEEGLFQLAQENLEHFQEDRDICLSILSLLWSLLVDVVTVDKEPLEQLSGMVTWVLATHP  
EDVEIAEAGCAVLWLLSLLGCIKESQFEQVVLLLSIQLC PGRVLLVNNAFRGLASLAK



## FIGURE 1Y

VSELVAFRIVVLEEGSSGLHLIQDIYKLYKDDPEVVENLCMLLAHLTSYKEILPEMESGG  
IKDLVQVIRGRFTSSLELISYADEILQVLEANAQPGLOEDQLEPPAGQEAPLQGEPLFRP

SEQ ID NO: 225\_018653.9\_H

GRGRGAGHARGLGRGPAGRRAPPRSLSRPGPGPGSRAGPAGRGEGSDAAPAGGSGRGFI  
RLLPAGLRPQORALRSGSEPPRPGQSPEPSPAPGAGRRGGRGELARQIRARYEEVQRYSRG  
GPGPGAGRPERRRLMDLAPGGPGLPRPRPPWARPLSDGAPGWPPAPGPGSPGPGPRLGCA  
ALRNVSGAQYMGSGYTKAVYRVRLPGGAVALKAVDFSGHDLGSCVREFGVRRGCYRLAA  
HKLLKEMVLLERLRHPNVLQLYGYCYQDSEDI PDTLTITELGAPVEMIQLLQTSWEDRF  
RICLSLGRLLHHLAHSPLGSVTLDFRPRQFVLVDGELKVTDLDDARVEETPCAGSTDCI  
LEFPARNFTLPCSAQGWCEGMNEKRNLNAYRFFFTYLLPHSAPPSLRPLLDIVNATGE  
LAWGVDETLAQLEKVLHLYRSGQYLQNSTASSSTEYQCIPDSTIPQEDYRCWPSYHHGSC  
LLSVFNLAEAVDVCESHAQCRAFVVTNQTWTGRQLVFFKTGWSQVVPDPNKTTYVKASG

SEQ ID NO: 226\_AA396601\_M

TRPGCAALRNVSGAQYVGSYTKAVYRVRLPGGAVALKAVDFSGHDLGSCVREFGARRG  
CYRLAAHKLLKEMVLLERLRHPNVLQLYGYCYQDSEGI PDTLTITELGAPVEMIQLLQTS  
SWEDRFRICLSLGRLLHHLAHSPLGSVTLDFRPRQFVLVNGELKVTDLDDARVEETPCT  
SSADCTLEFPARNFSLPCSAQGWCEGMNEKRNLNAYRFFFTYLLPHSAPPSLRPLLDIV  
VNATGELAWGVDETLAQLETALHLFRSGQYLQNSTSSRAEYQRI PDSAITQEDYRCWPSY  
HHGGCLLSVFNLAEAIDVCESHAQCRAFVVTNQTWTGRKLVFFKTGWNQVVPDAGKTTY  
VKAPG

SEQ ID NO: 227\_VRK3\_H

MISFCPCGKSIQAAFKFCPYCGNSLPVEEHVGSQTFVNPVHVSFQGSKRGLNSSFETSP  
KKVKSSTVTSPRLSLFSDGDSSESEDTLSSSERSKSGSGSRPPTPKSSPQKTRKSPQVTR  
GSPQKTSCSPQKTRQSPQTLKRSRVTTSLALPTGTVLTDKSGRQWKLKSFQTRDNQGI L  
YEAAPTSTLTCDSGPQKQKFSCLKDAKDGRLFNEQNFFQRAAKPLQVNKWKKLYSTPLLA  
IPTCMGFGVHQDKYRFLVPSLGRSLQSAALDVSPKHVLSERSVLQVACRLLDALEFLHEN  
EYVHGNVTAENIFVDPEDQSQVTLGAGYGFAYRYCPSGKHVAYVEGSRSPHEGDLEFISMD  
LHKGCGPSRRSDLQSLGYCMLKWLYGFLPWTNCLPNTEDIMKQKQKFVDKPGPFVGPCH  
WIRPSETLQKYLKVVMALTYEEKPPYAMLRNNLEALLQDLRVSPYDPIGLPMVP

SEQ ID NO: 228\_S71575\_M VRK3\_M

IPTCIGFGIHQDKYRFLVFP SLGRSLQSAALDDNPKHVVSERCVLQVACRLLDALEYLHEN  
EYVHGNLTAENVFVN PEDLSQVTLVGYGFTYRYCPGGKHVAYKEGSRSPHDGDLEFISMD  
LHKGCGPSRRSDLQTLGYCMLKWLYGSLPWTNCLPNTTEKITRQKQKYLDSPERLVGLCGR  
WNKASETLREYLKVVMALNYEEKPPYATLRNSLEALLQDMRVSPYDPLDLQMPV

SEQ ID NO: 229\_AA45427\_H

MGHALCVCSRGTVIIDNKRYLFIQKLGEFFSYVDLVEGLHDGHFYALKRILCHEQQDRE  
EAQREADMHRLFNHPNILLRLVAYCLRERGAKHEAWLLL PFFKRGTLWNEIERLKDKGNFL  
TEDQILWLLLGICRGLEAIAHAKGYAHRDLKPTNILLGDEGQPVLM DLGSMNQACIHVEGS  
RQALTLQDWAAQRCTISYRAPELFSVQSHCVIDERTDVWSLGCVLYAMMFGE GPYDMVFQ  
KGDSVALAVQNQLSIPQSPRHSSALRQLLNSMMTVDPHQRP HILLLSQLEALQPPAPGQ  
HTTQI

SEQ ID NO: 230\_H05721\_H

MAVRQALGRGLQLGRALLRFTGKPGRAYGLGRPGPAAGCVRGERPGWAAGPGAEP RRVG  
LGLPNRLRFFRQSVAGLAARLQRQFVVRWGCAGPCGRAVFLAFGLGLGLIEEKQAESRR

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## FIGURE 12

AVSACQEIQAIFTQKSKFGPDPLDTRRLQ3FRLEEYLIQSIGKGCSSAAVYEATMPTLPQ  
 NLEVTKSTGLLPGRGPGTSAPGEGQERAPGAPAFPLAIKMMWNI SAGSSSEA I LNTMSQE  
 LVPASRVALAGEYGAVTYRKS KRGPQLAPHPNI I RVLRAFTSSVPLLPGALVDYPDVLP  
 SRLHPEGLGHGRTLFLVMKNYPCTLRQYLCVNTPSPRLAAMMLLQLLEGVDHLVQQGIAH  
 RDLKSDN I LVELDPDGCPWLVIADFGCCLADESIGLQLPFSSWYVDRGGNGCLMAPEVST  
 ARPGPRAVIDYSKADAWAVGAIAYE I FGLVNPFGYGGKAHLESRSYQEAQLPALPESVPP  
 DVRQLVRALLQREASKRPSARVAANVLHLSLWGEHILALKNLKLDKMVGWLLQQSAATLL  
 ANRLTEKCCVETKMMLFLANLECETLCQAALLLCSWRAAL

SEQ ID NO: 231\_AI086865\_H

MEKYERIRVVGRGAFGI VHLCLRKADQKLVI I KQIPVEQMTKEERQAAQNECQVLKLLNH  
 PNVEIYYENFLEDKALMIAMEYAPGGTLAEFIQKRCNSLLEEETILHFFVQILLALHHVH  
 THLILHRDLKTQNILLDKHRMVVKIGDFGISKILSSKSTPCYISPELCEGKPYNQKSDIW  
 ALGCVLYELASLKRAFEAANLPALVLKIMSGTFAPISDRYSPELRQLVLSLLSLEPAQRP  
 PLSHIMAQPLCIRALLNLHTDGREVRGPQQHREQDHQCPLQRG I IMTFGSGSNGCLGHGS  
 LTDISQPTIVEALLGYEMVQQVEEALSFTLLGSAPLDQEPLLSIDLGTAHSAAVTGEEDL  
 GSGDVNRLPSWERGHLLAGVASSTDVSTFSEGDCKEPPDKCCWRHKQCTGHI I YPFASDCV  
 RHSLHLHSVNHCNCSRLKDSSSEDSSSSRGAGPTCSHVIESPCFELTPEEEHVERFRYGW  
 CKSYRPVSVAVIHHPLYHECGADDLNXXKKRKRKRKRKRKPP I PTQVGPATASPD LGTSMAT  
 GTPDSTAPIT I WRSESPTGKGQGSKVIKKVKKKKEKEKDKEEMDEKAKLKKKAKKGQLTK  
 KKSPVKLEPSPPDVSRSL SARQLARMSSESPESREELESEDSYNGRGQGELSSSEDI VESS  
 SPRKRENTVQAKKTGAKPSQARKVNKRKSPPGSNPNLS

SEQ ID NO: 232\_AA836348\_H

MSVLGEYERHCDSINSDFGSESGGCGDSSPGPSASQGPRAGGGAAEQEELHYIPIRVLGR  
 GAFGEATLYRRTEDDSL VVWKEVDLTRLSEKERRDALNEI V I LALLQHDNI I AYYNHFMD  
 NTTLLIELEYCNGGNLYDKILRQKDKLFEEEMVVWYLFQIVSAVSCIHKAGILHRDIKTL  
 NIFLTKANLIKLG DYGLAKKLNSEYSMAETLVGTPPYMSPELCQGVKYNFKSDI WAVGCV  
 IFELLTLKRTFDATNPLNLCVKI VQGIRAMEVDSSQYSLELIQM VHSCLDQDPEQRPTAD  
 ELLDRPLLKRRRSSTVTEAPIAVVTSRTSEVYVWGGGKSTPQKLDVIKSGCSARQVCAG  
 NTHFAVVTVKEKELYTWVNMQGGTKLHGQLGHGDKASYRQPKHVEKLQGKAIRQVSCGDDF  
 TVCVTDEGQLYAFGSDYYGCMGVDKVAGPEVLEPMQLNFFLSNPVEQVSCGDNHVVLTR  
 NKEVYSWGCGEYGRGLDSEEDYYTPQKVDVPKALI I VAVQCGCDGTFLLTQSGKVLACG  
 LNEFNKLGLNQCMGSI INHEAYHEVPYTTSTFLAKQLSFYKIRTIAPGKTHTA AIDERGR  
 LLTFGCNKCGQLGVGN YKKRLGINLLGGPLGGKQVIRVSCGDEFTIAATDEKVLNSKTIR  
 SNSSGLSIGTVFQSSSPGGGGGGGGGEEEDSQQESETPDPSGGFRGTMEADRGMEGLISP  
 TEAMGNSNGASSSCPGWLRKELENAEFIPMPDSPSPLSAAFSESEKDTLPYEELQGLKVA  
 SEAPLEHKPQVEASVTELF AFESQLVTSAESCSNLCWEGNTTDS SCVCVQLSAGGG

SEQ ID NO: 233\_R86668\_H, MKK6\_H

MNLLLSYRDVQDYS A I IELVETLQALPTCDVAEQHNVC FHYTFALNRRNRPGDRAKALSV  
 LLPLVQLEGSVAPDLYCMCGRIYKDMFFSSGFQDAGHREQAYHWYRKAFDVEPSLHSGIN  
 AAVLLIAAGQHFEDSKELRLIGMKLGCLLARKGCVEKMQYYWDVGFYLG AQ I LANDPTQV  
 VLAAEQLYKLNAPIWYLVSVMETFLLYQHFRPTPEPPGGPPRRAHFWLHFL LQSCQPFT  
 ACAQGDQCLVLVLEMNKV I LPAKLEVRGTDPVSTVTL SLLPETQDIPSSWTFPVASICG  
 VSASKRDERCCFLYALPPAQDVQLCFPSVGHCQWFCGLIQAWVTNPDSTAPAEAEAGAGE  
 MLEFDYEYTETGERLVLGKGT YGVVYAGRDRHTRVRIAIKEI PERDSRFSQPLHEEIALH  
 RRLRHKNIVRYLGSASQGGY LKIFMEEVPGGSLSSLLRSVWGPLKDNESTISFYTRQILQ  
 GLGYLHDNHI VHRDIKGDNLINTFSGLLKISDFGTSKRLAGITPCTETFTGT LQYMAPE  
 I IDQGPRGYGKAADIWSLGCTVIEMATGRPPFHELGSQAAMFQVGMVKVHPPMPSSLSA

## FIGURE 1AA

EAQAFLLRTFEPDPRLRASAQTLLGDPFLQPGKRSRSPSSPRHAPRPSDAPSASPTPSAN  
STTQSQTFFPCPQAPSQHPPSPPKRCLSYGGTSQLRVPEEPAAEEPASPEESSGLSLLHQE  
SKRRAMLAAVLEQELPALAENLHQEQKQEQGARLGRNHVEELLRCLGAHIHTPNRRQLAQ  
ELRALQGRLRAQGLGPALLHRPLFAFPDAVKQILRKRQIRPHWMFVLDLSLLSRAVRAALG  
VLGPEVEKEAVSPRSEELSNEGDSQQSPGQQSPLPVEPEQGPAPLMVQLSLLRAETDRLR  
EILAGKEREYQALVORALQRLNEEARTYVLAPEPPTALSTDQGLVQWLQELNVDSGTIQM  
LLNHSFTLHTLLTYATRDDLITYTRIRGGMVCRIWRAILAQRAGSTPVTSGP

SEQ ID NO: 234\_PAK6\_H

MFGKKKKKIEISGPSNFEHRVHTGFDPQEQQKFTGLPQQWHSLLADTANRPKPMVDPSCIT  
PIQLAPMKTIVRGNKPKETSINGLLEDFDNISVTRSNLSRKESPTPTDQGASSHGPGHA  
EENGFITFSQYSSSESDTTADYTTKEYREKSLYGDDLDPYRGSAAKQNGHVMKMKHGEA  
YYSEVKPLKSDFARFSADYHSHLDSLSKPSEYSDLKWEYQRASSSSPLDYSFQFTPSRTA  
GTSGCSKESLAYSESEWGPSLDDYDRPKSSYLNQTSPOPTMRQRSRSGSGLQEPMPFG  
ASAFKTHPQGHSYNSYTYPRLSEPTMCIPKVDYDRAQMVLSPLSGSDTYPRGPAKL PQS  
QSKSGYSSSSHQYPSGYHKATLYHHPSLQSSSQYISTASYLSSLSSSTYPPPSWGSSS  
DQQPSRVSHQFRAALQLVSPGDPREYLANFIKIGEGSTGIVCIATEKHTGKQVAVK KM  
DLRKQQRRELLFNEVVIMRDYHHDNVDMYSSYLVGDELWVMEFLEGGALTDIVTHTRM  
NEEQIATVCLSVLRALSYLHNQGVHRDIKSDSILLTSDGRIKLSDFGFCAQVSKEVPKR  
KSLVGTPYWMAPEVISRLPYGTEVDIWSLGIMVIEMIDGEPPYFNEPPLQAMRRIRDSL P  
PRVKDLHKVSSVLRGFLDLMLVREPSQRATAQELLGHPFLKLAGPPSCIVPLMRQYRHH

SEQ ID NO: 235\_SURTK106\_H

MNDRNEIQMEAKLQSLTIIAQEILCRFFITLRRHARFLCLKGRQGMARSGITHSCAVCI  
LCGPSREGDSPVAMGMTRMLLECSLSDKLCVIEKQYEVIIVPTLLVTIFLILLGVILWL  
FIREQRTQQQSRSGPQGIAPVPPPRDLSWEAGHGGNVALPLKETSVENFLGATT PALAKLQ  
VPREQLSEVLEQICSGSCGPIFRANMNTGDPSKPKSVILKALKEPAGLHEVQDFLGRIQF  
HQYLGKHKNLVQLEGCCTEKLPLYMVLEDVAQGDLLGFLWTCRRDVMTMDGLLYDLTEKQ  
VYHIGKQVLLALEFLQEKHLFHGDVAARNILMQSDLTAKLCGLGLAYEVYTRGAISSTQT  
IPLKWLAPERLLL RPASIRADVWSFGILLYEMVTLGAPPYPEVPPTSILEHLQRRKIMKR  
PSSCTHTMYSIMKSCWRWREADRPSPRELRLRLEAAIKTADDEAVLQVPELVPELYAAV  
AGIRVESLFYNYSML

SEQ ID NO: 236\_AA098024\_M

LQEKHLFHGDVAARNILIQSDLTPKLCHLGLAYEVHAHGAISSARSSTIPLKWLAPERLL  
LRPASIRGDIWSFGILLYEMVTLGAPPYPEVPPTSILQYLQRRKIMKRPSSCSHAMYNIM  
KCCWRWSEDSRPLLQVLLQRLAASRSADDKAVLQVPELVPELYADVAGIRAESISYSF  
SVL

SEQ ID NO: 237\_SGK2ALPHA\_H

MNSSPAGTPSPQPSRANGNINLGPSANPNAQPTDFDFLKVIGKGNYGKVLLAKRKSDGAF  
YAVKVLQKKSILKKKEQSHIMAERSVLLKNVRHPFLVGLRYSFQTPEKLYFVLDYVNGGE  
LFFHLQRRERRFLEPRARFYAAEVASAIGYLHSLNIIYRDLKPENILLDCQGHVVLTD FGL  
CKEGVEPEDTTSTFCGTPEYLAPEVLRKEPYDRAVDWWCLGAVLYEMLHGLPPFYSQDVS  
QMYENILHQPLQIPGGRTVAACDLLQSLLHKDQRQRLGSKADFLEIKNHVFFSPINWDDL  
YHKRLTPPFNPNTGPADLKHFDPEFTQEAVSKSIGCTPDTVASSSGASSAFLGFSYAPE  
DDDILDC

SEQ ID NO: 238\_CCRK\_H  
MDQYCILGRIGEGAHGIVFKAKHVETGEIIALKKKVALRRLEDGFPNQALREIKALQEMED  
NQYVVQLKAVFPHGGGFVLAFEFMLSDLAEVVRHAQRPLAQAQVKSYLEMLLKGVAFFCHA  
NNIVHRDLKPANLLISASGQLKIADFGGLARVFS PDGSRLYTHQVATRSVGCIMGELLNGS  
PLFPGKNDIEQLCYVLRILGTPNPQVWPELTEL PDYNKISFKEQVPMPL EEVLPDVSPQA  
LDLLGQFLLYP PHQRIAASKALLHQYFFTAPLPAHPSELPI PQRLGGPAPKAHPGPPHIH  
DFHVDRPLEGVAVEPRADSALHPGGVRSWPWSRLPAPQDHSVHLFLCHLPGFTLQGLPMA  
TVGPHHTLPLSPCEGWSRGRGHVPSQEYENIQSSRGDSWPVLGEPYLLCATDVPIRTVSS  
AASOGLHMND DACLG AASPECCLLVKEKCRE

SEQ ID NO: 239\_TESK2\_H  
MDRSKRNSIAGFPPRVERLEEFEGGGGGEGNVSQVGRVWPSSYRALISAFSRLTRLDDFT  
CEKIGSGFFSEVFKVRHRASGQVMALKMNTLSSNRANMLKEVQLMNRLSHPNILRYINS  
NLEQLLDSNLHLPWTVRVKLAYDIAVGLSYLHFKGIFHRDLTSKNCLIKRDENGYS  
AVVADFGLAEKIPDVSMGSEKLAVVGSPFWMAPEVLRDEPYNEKADVFSYGIILCEI  
IARIQADPDYLPRTENFGLDYDAFQHMVGDCPPDFLQLTFNCCNMDPKLRPSFVEIG  
KTLEEILSRLQEEQERDRKLQPTARGLLEKAPGVKRLSSLDDKIPHKSPCPRRTI  
WLSRSQSDIFSRKPPRTVSVLDPYYRPRDGAARTPKVNPFSARQDLMGGKIKFFDL  
PSKSVISLVFDLDAPGPGTMPLADWQEPLAPPIRRWRSLPGSPEFLHQEACPFVGR  
EESLSDGPPPRLLSSLKYRVKEIPFRASALPAAQAHEAMDCSILQEENGFGSRPQGT  
SPCPAGASEEMEVEERPAGSTPATFSTSGIGLOTQGKQDG



## FIGURE 2A

SEQ ID NO: 1\_X69117\_H BARK2\_H

ATGGCGGACCTGGAGGCCGTGCTGGCCGATGTCAGTTACCTGATGGCCATGGAGAAGAGC  
AAGGCGACCCCGGCCGCCCGCGCCAGCAAGAGGATCGTCCTGCCGGAGCCCAGTATCCGG  
AGTGTGATGCAGAAGTACCTTGCAGAGAGAAATGAAATAACCTTTGACAAGATTTTCAAT  
CAGAAAATTGGTTTCTTGCTATTTAAAGATTTTTGTTTTGAATGAAATTAATGAAGCTGTA  
CCTCAGGTGAAGTTTTATGAAGAGATAAAGGAATATGAAAACTTGATAATGAGGAAGAC  
CGCCTTTGCAGAAGTCGACAAATTTATGATGCCTACATCATGAAGGAACCTTCTTTCCTGT  
TCACATCCTTTCTCAAAGCAAGCTGTAGAACACGTACAAAGTCATTTATCCAAGAAACAA  
GTGACATCAACTCTTTTTTCAGCCATACATAGAAGAAATTTGTGAAAGCCTTCGAGGTGAC  
ATTTTTCAAAAATTTATGGAAAGTGACAAGTTCCTAGATTTTGTGTCAGTGGAAAAACGTT  
GAATTAAATATCCATTTGACCATGAATGAGTTCAGTGTGCATAGGATTATTGGACGAGGA  
GGATTTCGGGGAAGTTTATGGTTGCAGGAAAGCAGACACTGGAAAAATGTATGCAATGAAA  
TGCTTAGATAAGAAGAGGATCAAAATGAAACAAGGAGAAACATTAGCTTTAAATGAAAGA  
ATCATGTTGTCTCTTGTCAGCACAGGAGACTGTCCTTTCATTGTATGTATGACCTATGCC  
TTCCATACCCCGAGATAAACTCTGCTTCATCCTGGATCTGATGAACGGGGGCGATTTGCAC  
TACCACCTTTCACAACACGGTGTGTTCTCTGAGAAGGAGATGCGGTTTTATGCCACTGAA  
ATCATTCTGGGTCTGGAACACGTGCACAATCGGTTTTGTTGTCTACAGAGATTTGAAGCCA  
GCAAATATTCTCTTGGATGAACATGGACACGCAAGAATATCAGATCTTGGTCTTGCCTGC  
GATTTTTCCAAAAGAAGCCTCATGCGAGTGTTGGCACCCCATGGGTACATGGCTCCCGAG  
GTGCTGCAGAAGGGGACGGCCTATGACAGCAGTGCCGACTGGTTCTCCCTGGGCTGCATG  
CTTTTCAAACCTTCTGAGAGGTCACAGCCCTTTCAGACAACATAAAACCAAAGACAAGCAT  
GAAATTGACCGAATGACACTCACCGTGAATGTGGAACCTTCAGACACCTTCTCTCCTGAA  
CTGAAGTCCCTTTTGGAGGGCTTGCTTCAGCGAGACGTTAGCAAGCGGCTGGGCTGTCAC  
GGAGGCGGCTCACAGGAAGTAAAAGAGCACAGCTTTTTTCAAAGGTGTTGACTGGCAGCAT  
GTCTACTTACAAAAGTACCCACCACCCTTGATTCCTCCCCGGGGAGAAGTCAATGCTGCT  
GATGCCTTTGATATTGGCTCATTGATGAAGAGGATACCAAAGGGATTAAGCTACTTGAT  
TGCGACCAAGAACTCTACAAGAACTTCCCTTTGGTCATCTCTGAACGCTGGCAGCAAGAA  
GTAACGGAAACAGTTTATGAAGCAGTAAATGCAGACACAGATAAAATCGAGGCCAGGAAG  
AGAGCTAAAAATAAGCAACTTGGCCACGAAGAAGATTACGCTCTGGGGAAGGACTGTATT  
ATGCACGGGTACATGCTGAACTGGGAAACCCATTTCTGACTCAGTGGCAGCGTCGCTAT  
TTTTACCTCTTTCCAAATAGACTTGAATGGAGAGGAGAGGGAGAGTCCCGGCAAAATTTA  
CTGACAATGGAACAGATTCTCTCTGTGGAAGAACTCAAATTAAGACAAAAAATGCATT  
TTGTTTCAGAATAAAAGGAGGGGAAACAATTTGTCTTGCAATGTGAGAGTGATCCAGAGTTT  
GTGCAGTGGAAGAAAGAGTTGAACGAAACCTTCAAGGAGGCCAGCGGCTATTGCGTCGT  
GCCCCGAAGTTCCTCAACAAACCTCGGTCAAGTACTGTGGAGCTCCCAAAGCCATCCCTC  
TGTCACAGGAACAGCAACGGCCTCTGA

SEQ ID NO: 2\_AA144574\_M BARK2\_M

CTGCTTCGTAGTCTACAGAGACCTGAAGCCTGCGAACATCCTCCTAGATGAATATGGGCA  
CGTGAGGATATCGGATCTCGGCCTTGCTGTGATTTCTCCAAAAGAAGCCTCATGCCAG  
CGTGGGCACCCATGGGTACATGGCTCCCGAGGTGTTGCAGAAGGGAACGTGCTATGACAG  
CAGCGCCGACTGGTTCTCCCTGGGCTGTATGCTCTTCAAACCTTCTGCGGGGCCACAGCCC  
CTTCAGGCAGCATAAAACCAAAGACAAGCATGAGATAGACCGAATGACCCTGACCGTGAA  
CGTGCAGCTTCCAGATGCCTTCTCCCCTGAGCTGAGGTCCCTCTTAGAGGGTTTGCTCCA  
GCGGGACGTGAGCCAGCGGCTGGGCTGCGGAGGAGGAGGGGACGAGAGTTGAAGGAGCA  
CATCTTCTTCAAGGGCATTGACTGGCAGCATGTGTACTTACGGAAGTACCCGCCACCCCT  
AATCCCTCCTCGGGGAGAGGTCAACGCTGCAGATGCCTTCGATATCGGCTCCTTCGATGA  
GGAAGACACCAAAGGCATTAAGCTGTTGGACTGTGACCAGGACCTCTATAAGAACTTCCC  
ACTGGTGATCTCCGAGCGCTGGCAGCAAGAAGTGGTGGAGACCATCTATGACGCCGTCAA  
TGCTGATACTGATAAAATCGAGGCCAGGAAGAAGGCTAAAAATAAGCAACTTGGTCAAGA

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## FIGURE 2B

GSAAGATTACGCTATGGGGAAGGACTGCATCATGCACGGGTACATGCTGAAGCTGGGGAA  
CCCCTTTCTCACACAGTGGCAAAGACGCTATTTTTTACCTGTTCCCCAACAGACTGGAGTG  
GAGAGGAGAGGBCGAGTCTCGGCAAAGTCTACTGACCATGGAACAGATCATGTCTGTGGA  
GGAGACCCAGATTAAAGACAGAAAGTGCATCTTACTCAGGATAAAGGGAGGGGAAGCAATT  
TGTCTTGCAATGTGAGAGTGACCCCGAGTTTGCACAGTGGCTGAAGGAGCTGACCTGCAC  
CTTCAATGAGGCCCCAGAGACTGCTGCGCCGTGCCCCCAAATTCTTCAACAAACCACGGGC  
CGCCATCCTGGAGTTCTCCAAGCCACCACTGTGTACAGAAATAGCAGCGGCCTCTGAAC  
CACAGAGCAGCGGGGCTGAAGGAGGGGGCCCCAGCTCTTCAGCCCAGGAGTGGAACGAAG  
CCACGGGGGAACCGTGTGGGGCTAAGACACAGTGTTTCTGAGCACTGACGGGGCTGCTCCA  
AGCCGAGGAGGCTCAGGACACCAGGGCGGCCTTCTGGGAGCTGGGACATCCTCGGGGCTG  
TCCTATCCACACTCGAAATTACTGAAGAAGCAGAGGCATTCTGCTGTG

SEQ ID NO: 3\_AA826850\_H

GAAGAGGATGGGCTCGTCCATGTGCGCGGCCACCGCGCGGAGGCGCGGTGTTTGACGACAA  
GGAGGACGTGAACTTCGACCACTTCCAGATCCTTCGGGGCATTGGGAAGGGCAGCTTTGG  
CAAGGTGTGCATTGTGCAGAAGCGGGACACGGAGAAGATGTACGCCATGAAGTACATGAA  
CAAGCAGCAGTGCATCGAGCGCGACGAGGTCCGCAACGTCTTCCGGGAGCTGGAGATCCT  
GCAGGAGATCGAGCACGTCTTCTGGTGAACCTCTGGTACTCCTTCCAGGACGAGGAGGA  
CATGTTTCATGGTTCGTGGACCTGCTACTGGGCGGGGACCTGCGCTACCACCTGCAGCAGAA  
CGTGCAGTTCTCCGAGGACACGGTGAGGCTGTACATCTGCGAGATGGCACTGGCTCTGGA  
CTACCTGCGCGGGCCAGCACATCATCCACAGAGATGTCAAGCCTGACAACATTCTCCTGGA  
TGAGAGAGGACATGCACACCTGACCGACTTCAACATTGCCACCATCATCAAGGACGGGGGA  
GCGGGCGACGGCATTAGCAGGCACCAAGCCGTACATGGCTCCGGAGATCTTCCAXTCTTT  
TGTCAACGGCGGGACCGGCTACTCCTTCGAGGTGGACTGGTGGTTCGGTGGGGGTGATGGC  
CTATGAGCTGCTGCGAGGATGGAGGCCCTATGACATCCACTCCAGCAACGCCGTGGAGTC  
CCTGGTGCAGCTGTTTCAGCACCGTGAGCGTCCAGTATGTCCCCACGTGGTCCAAGGAGAT  
GGTGGCCTTGCTGCGGAAGCTCCTCACTGTGAACCCCGAGCACCGGCTCTCCAGCCTCCA  
GGACGTGCAGGCAGCCCCGGCGCTGGCCGGCGTGCTGTGGGACCACCTGAGCGAGAAGAG  
GGTGGAGCCGGGCTTTCGTGCCCAACAAAGGCCGTCTGCACTGCGACCCACCTTTGAGCT  
GGAGGAGATGATCCTGGAGTCCAGGCCCTGCACAAGAAGAAGAAGCGCCTGGCCAAGAA  
CAAGTCCCGGGACAACAGCAGGGACAGCTCCAGTCCGAGAATGACTATCTTCAAGACTG  
CCTCGATGCCATCCAGCAAGACTTCGTGATTTTTTAACAGAGAAAAGCTGAAGAGGAGCCA  
GGACCTCCCGAGGGAGCCTCTCCCCGCCCCCTGAGTCCAGGGATGCTGCGGAGCCTGTGGA  
GGACGAGGCGGAACGCTCCGCCCCTGCCCATGTGCGGGCCCCATTTGCCCCCTCGGGCGGGAG  
CGGCTAGGCCGGGATGCCCGTGGTCTCACCCCTTGAGCTGCTTTGGAGACTCGGCTGCC  
AGAGGGAGGGCCATGGGCCGAGGCCTGGCATTACGTTCCACCCAGCCTGGCTGGCGGT  
GCCACAGTGCCCCGGACACATTTACACCTCAGGCTCGTGGTGGTGCAGGGGACAAGAG  
GCTGTGGGTGCAGGGGACACCTGTGGAGGGCATTTCCCGTGGGCCCCCGAGACCCGCCTA  
GATGGAGGAAGCGCTGCTGGGCGCCCTCTTACCGCTCACGGGGAGCTGGGGCCATGGATG  
GGACAGGAGTCTTTGTCCCTGCTCAGCCCGGAGGCTGTGCACGGCCCTCGTCACAAGGTG  
ACCCTTGACGACAGGCCGCGGGTGCCCCAGGCTCGGCTCAGTTCTTGGAGGTCAAGGGC  
ATGGGTTGGGGTAGTGGGTGGGGAGGTGAATGTTTTCTAGAGATTCAAACCTGCTCCAGCA  
ATTTCTGTATAGTTTTTCACCTCTGAGAATTACAATGTGAGAACCGCTC

SEQ ID NO: 4\_AA960957\_H

GTCCACATCCCGCATCCGGCATCCAGCGGGCCGGGCATGTAGCAGCGGCAGCAACGGCG  
GAATATGGGCGGGGAACCACTCCCAAGCCCCCGTGTTTGACGAGAATGAGGAAGTCAA  
CTTTGACCATTTTTCAGATTCTGCGGGCCATTGGTAAAGGGAGTTTTTGGAAAGGTATGCAT  
CGTGCAGAAGCGAGACACTAAGAAAATGTATGCAATGAAGTACATGAACAAGCAGAAGTG  
CATCGAGAGGGATGAGGTTCCGAATGTTTTCCGGGAGCTGCAGATCATGCAAGGGCTGGA

## FIGURE 2C

GCACCCCTTCCTGGTCAATCTGTGGTACTCCTTCCAGGATGAGGAGGACATGTTTCATGGT  
GGTGGACCTGCTCCTGGGAGGCGACCTGCGCTACCATCTGCAGCAGAATGTGCATTTTCAC  
AGAGGGGACTGTGAAACTCTACATCTGTGAGCTGGCACTGGCCCTGGAGTATCTTCAGAG  
GTACCACATCATCCACAGAGACATCAAGCCAGACAATATCCTGCTGGATGAACACGGACA  
TGTTTCACATTACAGACTTCAACATAGCGACGGTAGTGAAAGGAGCAGAAAGGGCTTCCTC  
CATGGCTGGCACCAAGCCCTACATGGCTCCAGAAGTATTCCAGGTGTACATGGACAGAGG  
CCCCGGATACTCGTACCCTGTGCGACTGGTGGTCCCTGGGCATCACAGCCTATGAGCTGCT  
GCGGGGCTGGAGGGCCGTACGAAATCCACTCGGTACGCCCCATCGATGAAATCCTCAACAT  
GTTCAAGGTGGAGCGTGTCCACTACTCCTCCACGTGGTGCAAGGGGATGGTGGCCCTGCT  
GAGGAAGCTCCTGACCAAGGATCCTGAGAGCCGCGTGTCCAGCCTTCATGACATACAGAG  
CGTGCCCTACTTGGCCGACATGAACTGGGACGCGGTGTTCAAGAAGGCACTGATGCCCCG  
CTTTGTGCCCCAATAAAGGGAGGTTGAACTGCGATCCCACATTTGAGCTTGAAGAGATGAT  
TCTAGAATCCAAGCCACTTCACAAAAAGAAGAAGCGATTGGCAAAGAACAGATCCAGGGA  
TGGCACAAGGACAGCTGCCCCGTGAATGGACACCTGCAGCACTGTTTGGAGACTGTCCG  
GGAGGAATTCATCATATTCAACAGAGAGAAGCTCAGGAGGCAGCAGGGACAGGGCAGCCA  
GCTCTTGGACACCGACAGCCGAGGGGGAGGCCAGGCCCAAAGCAAGCTCCAGGACGGGTG  
CAACAACAACCTCCTCACCCACACCTGCACCCGTGGCTGCAGCAGCTGAGCCCACACTTG  
TTGCTGCTCAACAGGACTGCACTCGTCTCTGCCCTGCCACCCAGAGCCCCCTCTTTGTGC  
CCTGATGGTCCCTGTCTCACCCCTGAAAACATCAGATGCAGAAAAAGCCCTGGACTTGGA  
GCTGGGAAGCCTGGGTTCTGGTCCCATCTCCATGACTGATTACGTGTGACCTCAGACAA  
GTCACGCCCTCTCTGTGCCTCCGTTTTCTGCATCTGCCAAAGGGGTAAACACTTCTGCC  
CCACTTCAAATTACAAGATTATGGGGAGAACCCAATTAGGTAGGAAACATGAAAAACCTT  
TGATATTTATAAAATCATTTTTTACGTGCAAAATATAACCTTAATATTTGAAGTGACCCCC  
ATTCCCCAAAGCAATCAAACCGTCATGACTTTGCAATTTGGCACATCCTAGCTTGTTAGA  
GGGCACTTCCGAAAAACACAGCCCTGACAGCAAAATAAAGGTCTGATATGTTGGCCCCCTT  
CTATGGAAACAACGCTGCCAAATCCTGGAGCAAAACCTGAAGTGTCTTCATGTGCATTCT  
CTGGCAGGCCACAGTCCTGAGCTTGTAAGATGGTGCAGCATGCAGACCAGACTTGTCCCC  
AAGGTCTCAGCGCTGCGGTCTCACTCCTCCCCTCATTTAAGAAGACTATCCTTACCTTTT  
AGTTTCAGCAGTCCTCACCACCACCATATCCCCAGTGCTGGGATGGCACACAGGTGTCCA  
TTCAGATGAGAGTTGGGTGCTGAGCATTTGGTTACTCCTGCAGAGTGTAATCAGCACCCCC  
ATCCAACCTGGCCCGAAAGCCCAGACCTGCAGCAGAACTCTCCAACCTCTCTATCAGCTTTC  
AGGGTTTTCTCTCCTGGGAAGGGTGTAATAATCAGCTTGTGAGATTCTTCTTACAGAGAGT  
ATCCAATCGGTATTGGTGGAGCGGCTCCCTATTTATACAATAGGAAGCATGGGTGCTTAG  
AAAGTTTTATTTTCAGGAGGAAAATGGGTTACACAAAAAGCAAACACTACATTCTGATCTGCT  
CAGGGAGAAGCTTGCCCTTTGAACTGGAAGATGTTGGGATGAGCAGGGAAAGCTTAGACTT  
TGGAGTCAGGTTTGTGTTTCAGAATCCAGCCCTGCTGGCTACTAACTAACTGGGAGACCTT  
AGGCAAAGCATGCAATCGCTCTGAATGGCAGTTTCTCATTTTTTAAACAGGGATAATAAA  
ACTAATATTGCAGGGGAGTTACAGGGTTAAATAAGATCCTGTGTGTAACCCCAAGCATTG  
GATGACTCATAGAATGGCCTTTTTTTGTGAGCATAATCGTCATCATTATTTAGATACTTTC  
TTCCTTCACTCACCCAGCAGGTGAGTTTTCTGTGCAAAACAAACCTGTTTAGGATTCTTCC  
AAATGTTCTTCTGGGGTCTTTGATATTTGTTTGTACATCCTGCTGAAGTTCGACTGTG  
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GCTGTCCATGTCATCTCTTAGATTTCTTAAAAGACATTTTAATGTATGGTTAGGTTTTAT  
ATTTTTATTTTTTAAAAAAGAAATAGTCAGTGTTTTTCTCCTTTCAACCGAGACTATTTTC  
TGGATTGTGTGCTCCTCGTCAGTTGACTTGTTTTGCACACTTTTCTTTACTTCATGTCCC  
CATCAACAACCGTCCTGCTCCCCACCTCCCCCAGGAAATAAGGGGCTGCTCCTCTCCCT  
ACTGTGACCCTGGAGGCTCTTAAGATGATGATGGTTTTTTTTTATTGGGCTGAGTTCACGA  
ATTAGGGGCAGGAGCTGGAAGTCGCCCTAGGAACACCAGATTTCTGGTTCTGTTCAAGT  
TGGCATTTCTTGTGTTGGAATAAACTATTTCTTGGACATTCCTTC

## FIGURE 2D

SEQ ID NO: 5\_TBK1\_H

TCCTGAGTCTCGAGGAGGCCCGGGAGCCCCGCCGGCGGGTGGCGCGGGCGGAGACCCGGGCTG  
GTATAACAAGAGGATTGCTTGATCCAGCCAAGATGCAGAGCACTTCTAATCATCTGTGGC  
TTTTATCTGATATTTTAGGCCAAGGAGCTACTGCAAATGTCTTTCGTGGAAGACATAAGA  
AAACTGGTGATTTATTTGCTATCAAAGTATTTAATAACATAAGCTTCCTTCGTCCAGTGG  
ATGTTCAAATGAGAGAATTTGAAGTGTTGAAAAAACTCAATCACAAAAATATTGTCAAAT  
TATTTGCTATTGAAGAGGAGACAACAACAAGACATAAAGTACTTATTATGGAATTTTGTG  
CATGTGGGAGTTTATACACTGTTTTAGAGAAGACCTTCTAATGCCTATGGACTACCAGAAT  
CTGAATTCTTAATTGTTTTGCGAGATGTGGTGGGTGGAATGAATCATCTACGAGAGAATG  
GTATAGTGCACCGTGATATCAAGCCAGGAAATATCATGCGTGTTATAGGGGAAGATGGAC  
AGTCTGTGTACAAACTCACAGATTTTGGTGCAGCTAGAGAATTAGAAGATGATGAGCAGT  
TTGTTTTCTCTGTATGGCACAGAAGAATATTTGCACCCTGATATGTATGAGAGAGCAGTGC  
TAAGAAAAGATCATCAGAAGAAATATGGAGCAACAGTTGATCTTTGGAGCATTGGGGTAA  
CATTTTACCATGCAGCTACTGGATCACTGCCATTTAGACCCTTTGAAGGGCCTCGTAGGA  
ATAAAGAAGTGATGTATAAAATAATTACAGGAAAGCCTTCTGGTGCAATATCTGGAGTAC  
AGAAAGCAGAAAATGGACCAATTGACTGGAGTGGAGACATGCCTGTTTTCTTGCAGTCTTT  
CTCGGGGTCTTCAGGTTCTACTTACCCCTGTTCTTGCAAACATCCTTGAAGCAGATCAGG  
AAAAGTGTTGGGGTTTTTGACCAGTTTTTTTGAGAACTAGTGATATACTTCACCGAATGG  
TAATTCATGTTTTTTTCGCTACAACAAATGACAGCTCATAAGATTTTATATTCATAGCTATA  
ATACTGCTACTATATTTTCATGAACTGGTATATAAACAACCAAAATTTCTTCAAATC  
AAGAACTTATCTACGAAGGGCGACGCTTAGTCTTAGAACCTGGAAGGCTGGCACAACATT  
TCCCTAAAACTACTGAGGAAAACCCTATATTTGTAGTAAGCCGGGAACCTCTGAATACCA  
TAGGATTAATATATGAAAAAATTTCCCTCCCTAAAGTACATCCACGTTATGATTTAGACG  
GGGATGCTAGCATGGCTAAGGCAATAACAGGGGTGTGTGTTATGCCTGCAGAATTGCCA  
GTACCTTACTGCTTTATCAGGAATTAATGCGAAAGGGGATACGATGGCTGATTGAATTAA  
TTAAAGATGATTACAATGAACTGTTCAAAAAAGACAGAAGTTGTGATCACATTGGATT  
TCTGTATCAGAAACATTGAAAAAACTGTGAAAGTATATGAAAAGTTGATGAAGATCAACC  
TGGAAGCGGCAGAGTTAGGTGAAATTTAGACATACACACCAAATTTGTTGAGACTTTCCA  
GTTCTCAGGGAACAATAGAAACCAGTCTTCAGGATATCGACAGCAGATTATCTCCAGGTG  
GATCACTGGCAGACGCATGGGCACATCAAGAAGGCACTCATCCGAAAGACAGAAATGTAG  
AAAACTACAAGTCCTGTTAAATTGCATGACAGAGATTTACTATCAGTTCAAAAAAGACA  
AAGCAGAACGTAGATTAGCTTATAATGAAGAACAAATCCACAAATTTGATAAGCAAAAAC  
TGTATTACCATGCCACAAAAGCTATGACGCACTTTACAGATGAATGTGTTAAAAAGTATG  
AGGCATTTTTTGAATAAGTCAGAAGAATGGATAAGAAAGATGCTTCATCTTAGGAAACAGT  
TATTATCGCTGACTAATCAGTGTTTTTGATATTGAAGAAGAAGTATCAAAATATCAAGAAT  
ATACTAATGAGTTACAAGAACTCTGCCTCAGAAAATGTTTACAGCTTCCAGTGGAATCA  
AACATACCATGACCCCAATTTATCCAAGTTCTAACACATTAGTAGAAATGACTCTTGGTA  
TGAAGAAATTAAAGGAAGAGATGGAAGGGGTGGTTAAAGAACTTGCTGAAAATAACCACA  
TTTTAGAAAGGTTTGGCTCTTTAACCATGGATGGTGGCCTTCGCAACGTTGACTGTCTTT  
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TTAAATGAATGCCTTTATAGATAGTCACTTGTTTCTACAATCCAGTATTTGATGTGGTGG  
TGTAATATGTACAATATTGTAAATACATAAAAAATATACAAATTTTTTGGCTGCTGTGAA  
GATGTAATTTTATCTTTTAACATTTATAATTATATGAGGAAATTTGACCTCAGTGATCAC  
GAGAAGAAAGCCATGACCGACCAATATGTTGACATACTGATCCTCTACTCTGAGTGGGGC  
TAAATAAGTTATTTTCTCTGACCGCCTACTGGAAATATTTTTTAAGTGGAACCAAAATAGG  
CATCCTTACAAATCAGGAAGACTGACTTGACACGTTTGTAAATGGTAGAACGGTGGCTAC  
TGTGAGTGGGGAGCAGAACCGCACCACTGTTATACTGGGATAACAATTTTTTTTGAGAAGG  
ATAAAGTGGCATTATTTTATTTTACAAGGTGCCCAGATCCCAGTTATCCTTGTATCCATG  
TAATTTTCAGATGAATTATTAAGCAAACATTTTAAAGTGAATTCATTATTA AAAA ACTATT  
ATTTTTTTCCTTTGGCCATAAATGTGTAATTGTCATTAAATTTCTAAGGTCATTTCAACT



## FIGURE 2E

GTTTAAAGCTGTATATTTCTTTAATTCTGCTTACTATTTTCATGGAAAAAATAAATTTCT  
CAATTTTAAAAAA

SEQ ID NO: 6\_AA305176\_H

TGGCTGCTCGCGGAGGGGCAGTGTACGCGGGGCCGCTGTAGGCTGTCCAGCGATGGATCC  
CACCGCGGGAAGCAAGAAGGAGCCTGGAGGAGGCGCGGCGACTGAGGAGGGCGTGAATAG  
GATCGCAGTGCCAAAACCGCCCTCCATTGAGGAATTCAGCATAGTGAAGCCCATTAGCCG  
GGGCGCCTTCGGGAAAGTGTATCTGGGGCAGAAAGGCGGCAAATTGTATGCAGTAAAGGT  
TGTTAAAAAAGCAGACATGATCAACAAAAATATGACTCATCAGGTCCAAGCTGAGAGAGA  
TGCCTGGCACTAAGCAAAAGCCCATTTCATTGTCCATTTGTATTATTCCTGCACTGCTGC  
AAACAATGTCTACTTGGTAATGGAATATCTTATTGGGGGAGATGTCAAGTCTCTCCTACA  
TATATATGGTTATTTTGATGAAGAGATGGCTGTGAAATATATTTCTGAAGTAGCACTGGC  
TCTAGACTACCTTCACAGACATGGAATCATCCACAGGGACTTGAAACCGGACAATATGCT  
TATTTCTAATGAGGGTCATATTAAGTACGCGATTTTGGCCTTTCAAAGTTACTTTGAA  
TAGAGATATTAATATGATGGATATCCTTACAACACCATCAATGGCAAAACCTAGACAAGA  
TTATTCAGAACCCAGGACAAGTGTATCGCTTATCAGCTCGTTGGGATTTAACACACC  
AATTGCAGAAAAAATCAAGACCCTGCAACATCCTTTACGCCTGTCTGTCTGAAACATC  
ACAGCTTTCTCAAGGACTCGTATGCCCTATGTCTGTAGATCAAAGGACACTACGCCTTA  
TTCTAGCAAATTACTAAAATCATGTCTTGAAACAGTTGCCTCCAACCCAGGAATGCCTGT  
GAAGTGTCTAATTCTAATTTACTCCAGTCTAGGAAAAGGCTGGCCACATCCAGTGCCAG  
TAGTCAATCCACACCTTCATATCCAGTGTGGAATCAGAATGCCACAGCAGTCCCAAATG  
GGAAAAGATTGCCAGGTTTGAGGGACATTTATCTTAATGAAAATCAATTATGTATGTCA  
AATGAATGTGAGAAATATTATACCTTTTCATATAAATTCCATAAGAAATGAAATTGTTA  
CATGAATGGCAGTCATAGTATTAATCAGAAATTCATTTTCTGCACATTCTGTCAAATTC  
TTTTGAAATATTTCAATTTCTCATTCAATTGTGACATTGTTCTTACTTGATTATATAATGA  
GATTCTTGCAGTAAATTGATAATAAATGCTTGGCTTCTGTGTATCTAGGTGGACCTCACT  
TGTTTTTAGAAGTCCTTCCCATGATACAGACATTGGCTTGTGTTTTGTTTTATTTTGT  
TTTTAACATATGTCATTTAAAACTCATATTACCTCCTTTT

SEQ ID NO: 7\_AA116841\_M

CCACGCGTCCGATCCCATGGCCAGAAGGCGAAGAAAAGCTATCTGATAATGCTCAAAGTG  
CAATGGACATGCTTTTAACCATTGATGATTCAAAGAGAGCTGGAATGAGAGAACTAAAC  
AGCATCCTCTCTTCAGTGAAGTGGACTGGGAAAATCTGCAGCATCAGACTATGCCTTTCTG  
TACCCCAACCAGACGACGAAACAGATACATCCTATTTTGAAGCCAGAAATAATGCTCAAC  
ATCTGACCGTATCTGGGTTTAGTCTGTAGCACATGCGTGTCAATTTTATCTAACTTGTGA  
TATAGAATTAAGTTTTACAGTAATATGCTACTTAATACTAGATTGGTCTAAATGGGATAA  
AAGTCATTATTTTACCCAGACTGAACAGCTTTTAATTACTAAGTACAACAGTTTTTACAG  
AATTAAATACTATAAGCAATATAATCAGTAATTAATCTTTACCTTAGAACTGTATATAA  
GCCATAATAGCTTTTTTTCATCTTATTTATTCCTGCACTTTATGAAGAGCAAAGTATCAA  
TAACTAAACACTACCACTCTAAATAGAGGGAGTGAGCCGT

SEQ ID NO: 8\_AA256100\_H

AGGGAGCTGACGGGCGCCCGGCCGGCTGCGGTCCGTGCGGAGGCTGAGCCGGCCGCGGGC  
GCGACCGGAGGCAGTTTCCGTTACTATGGCAATGACGGCAGGGACTACAACAACCTTTCC  
TATGAGCAACCATACCCGGGAAAGAGTGAAGTGTAGCCAAGCTCACATTGGAGAATTTTAA  
TAGCAACCTAATTTTACAGCATGAAGAGAGAGAAACCAGGCAGAAGAAATTAGAAGTGGC  
CATGGAAGAAGAAGGATTAGCAGATGAAGAGAAAAAGTTACGTCGATCACAACACGCTCG  
CAAAGAAACAGAGTTCTTACGGCTCAAAGGACCAGACTTGGCTTGGATGACTTTGAGTC  
TCTGAAAGTTATAGGAAGAGGAGCTTTTGGAGAGGTGCGGTTGGTCCAGAAGAAAGATA  
AGGCCATATCTATGCAATGAAGATATTGAGAAAGTCTGATATGCTTGAAAAAGAGCAGGT

FIGURE 2F

GGCCCATATCCGAGCAGAAAGAGATATTTTGGTAGAAGCAGATGGTGCCTGGGTGGTGAA  
GATGTTTTACAGTTTTTCAGGATAAGAGGAATCTTTATCTAATCATGGAATTTCTCCCTGG  
AGGTGACATGATGACATTGCTAATGAAGAAAGACACCTTGACAGAAGAGGAAACACAGTT  
CTACATTTTCAGAGACTGTTCTGGCAATAGATGCGATCCACCAGTTGGGTTTTCATCCATCG  
GGATATTAAGCCAGACAACCTTTTATTGGATGCCAAGGGTCATGTAAAATTATCTGATTT  
TGGTTTATGTACGGGATTAAAGAAAGCTCACAGGACTGAATTTTATAGAAATCTCACACA  
CAACCCACCAAGTGACTTCTCATTTCAGAACATGAACTCAAAGAGGAAAGCAGAAACTTG  
GAAGAAGAACAGGAGACAACCTGGCATATTCCACAGTTGGGACACCAGATTACATTGCTCC  
AGAAGTATTCATGCAGACTGGTTACAACAAATTGTGTGACTGGTGGTCTTTGGGAGTGAT  
TATGTATGAAATGCTAATAGGATATCCACCTTTCTGCTCTGAAACACCTCAAGAAACATA  
CAGAAAAGTGATGAACTGGAAAGAACTCTGGTATTTCTCCAGAGGTACCTATATCTGA  
GAAAGCCAAGGACTTAATTCTCAGATTTTGTATTGATTCTGAAAACAGAATTGGAAATAG  
TGGAGTAGAAGAAATAAAAGGTCATCCCTTTTTTTGAAGGTGTCGACTGGGAGCACATAAG  
GGAAAGGCCAGCAGCAATCCCTATAGAAATCAAAGCATTGATGATACTTCAAATTTTGA  
TGACTTCCCTGAATCTGATATTTTACAACCAGTGCCAAATACCACAGAACCGGACTACAA  
ATCCAAAGACTGGGTTTTTCTCAATTATACCTATAAAAGGTTTGAAGGGTTGACTCAACG  
TGGCTCTATCCCCACCTACATGAAAGCTGGGAAGTTATGAATGAAGATAACATTCACCCA  
TAACCAAGAGAACTCAGGTAGCTGCATCACCAGGCTTGCTTGGCGTAGATAACAATACAC  
TGAAATACTCCTGAAGATGGTGGTGCTTATTGACTACAAGAGGAAATTCTACAGGATTAG  
GATTTCTAAGACTACTATAGGAATTGGTTGGCAGTGCCAGCTGGCTCTTTTTTTTTTAATAT  
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ATCAGTAAAAGCCATCTTCCATAGTTGGTGTAGAACATTGCCCTATTGGTTTGGACATC  
TGTAGAATATATATGAAGACAATTTCTGTAATGGTTTTTAAGAGATTTAAAAAGAAATTCA  
CTGGTTCTTTACAAAATAGAATTTATCATCAAGTTATTACACAACTTCACAGTAAGGAG  
TGACAAGTTTATAATAAGGAAGACAAAGTTTAACACCTTCACTCAAGCACTCCACTAATA  
TATTTACGTTGCATTCAGAAATACTGATGACCTTCATATACGTAGTCTGTATACTCATAG  
GGAGATGTACTGTATTATATAACATGTAAAGTTGATTTTCTTGTGACAAGAGAACTTCTT  
TTTTTAACAAGAGGACATGGCATTATTTTAATTTGATTATGGTGAGTTGAATTTAAGACA  
TGACCATGAAGGCTGCTTGTAGAATTAGTGTATTTTTTATTAACTATTTTTTTTAAATGTC  
AACTTCTATCATGTAAATGGACTTATAGAGAACAAAAAGCTATTTACTTTGGTTTTCTA  
GAAAGTTGTTACATATCATGGCTGGTTAACTTTTATTTCTTTTGATGAAAATTTTTCCTT  
TGATAGTACTTGTATTATTGTGCCATTATTTTCTTATGCTCCAAATGTACCAAAGATCTT  
GAACAGAGTGGATGTTCACTGAGTAGAATTTTCTTTCTGTGGGCATGCTGTATTC  
AGACCTGACAGATCTTTGATAGAGGTCAGCTTATTAAAGGGCAATATTGTTCTTGTTTAG  
CTACATCACTGTGGTGAATATAGATGGAATTAAGGAAGTAAATGCAGGCCAGGGGGTGT  
GATGAGAGGATAGGGGAGATAATATCAGCATCAAATTTCTTTGGGTATCTCTCTAAGAATT  
AAATAATCTTTTCTAGCTTAATATTTTAATTCTAATTCAAACAACTCTGAGGTTTTGGTT  
TCATTAGTAATAGTTGAGGAATAATACTAGCAAAGAATGGCCTAATGTTTGTGCATAAC  
TGTTAATGGATGAAATTTTTTAAAGATACAACCATGATAACCATTATAAATGATCTATGA  
TCAAATCTAAAGTGATGAATTATTTGTAGGAATGTCTTCCTAATGGGGAAGAATTGCAT  
AGGAGCATTATGCAAATCTACACAAGCTTTTATAAATGTTGCTGCTGGGTAGCTCCACAG  
TGTTTCATAAGGCCATCCTGTTTCCCCCACTCCCCCATTTTTGGTTTTGTTTCTTTTTAA  
ATATTTGTTGAGTACTTACGTGTTTATCTAACAGTTCACTTCCATTTTTCTAGTCTGGAT  
TTTTTGAGTATTTAGGAAAGAGAGCTATTAAAACTCTGGGGATTTCTCAATGTGACTAA  
CTCTAATTTTTCTAATTATACTGCCTTTAATTAAACATAATATTAACTTTTGCTGAGGTT  
TATGAGATTTTCTCACCCACATCGCTCCCTTTTTTTTAAAGGACTGTTTTGCTAGTG  
TGATAATGAATAGGTAAGATATGAGATAATTGCAACATTGTCCTAGTTCTAGTATGGTAA



## FIGURE 2G

CTATTCTTGAAATGGTATTGAAAAATACCGTTAATTCAAATTGACAGAGATTGATAAAAA  
GAAACTGATTTACCTAAGTTTACTTTTTTAATTGCATAATAGAGCATTTTTTTGTTTTGAGT  
TCCCTCATTCTTATTACCAGAAAGAGCTTGCAAATAGTTTTACTTTCTTGGCACTGGAAG  
GGTAGTTCTGGAAAGCTACTTTGTTGAGAGTCTCATTCTTCCCTGGAGTTAATAGAGTGA  
TTCACAATCTTTGGGGTTTTCTCCTCATCAAAGCATTTCTTAAGTGCCTATCTAAAAGC  
AATTAAAGACTGTGTCTGCCCTTTAGAAGCTAAGAATTTGATTCATGATGCAAATTAAC  
AGATAATTTGCAAAGTACCCTTGAGATTGAATTTTCTCTATTATATATTTCCCATATTTT  
AGGTGAATAATTTAATTTAAATGACAAAACCTATCTAGTCAACTGGGCATAATGACATT  
TTCTTTAAATTAGACTCTATTTTGAATTAAAAGAGTTTTATTATAAACCGTGTGTTTTT  
GTTTTTCTAAGTATATAGAAAGCTTGTATAATTCAGATTTATCAATTTCTGATTTAATG  
TAGACTTTGACTTTTTTTATTAAAAACCTTTGTATTAAAGCAAGTTATGTTATTTTTCTTT  
TATGCATTTATTACTAACATAGCTTTAAATCTTTAAATGTATTGAAGCATTGTGCTGTCT  
GAAAATAAGGAATTGCTTATAAACCCAGCCACTTCTGAATACAATATGTAGCTGATTTAAT  
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GCCTAAGATAGGGTTTCATTTATTTCTATACTTTTTCTGTTTTTTTAAACACCTGCATATT  
TTTATGTAAATCTCTAAATTTAAAATATTTTAAAGTACATTTATTTTTGGTGTTTTTATTGT  
ATAAACCTTAGACAATCAATCAGTCAGTCTTTACTGACAGGAGCAGCAGCTATCTGTCT  
TTTGCTGATCTACAAATAAATGAATTGAGAATTTAGTCCATAGAGGTCCCTGGCTACCAA  
ACACATTCTCCTTTGAATTGTTAAAATTCAGAACATTCAAATAACTGTTTTGCTACAAAC  
CCATGATTATTTTCTGTTGTGTTTATTTAAATTTACTTTCTCTTTAGAAGTGCACCTTAT  
TTCTGAAAAATCTTAATGAAACAAACGCTTAGAACAAATATAAATATGAGACACTTGGGA  
CTACTAGAGATATTTTAGATTTTTTATGAAAAAAATGTGAGGGGATATTGCTGCTTTAAAA  
AGGAATAAGTAATAAAAAATATATCTCAGCTATTTTTTTTAAAGCAATATAATTCAGCAAT  
TGTCTAGAAAAGTAATCATGAGGCTACTGAGTTTGGTGTTCAGTTACTGAGTTTCAAAAA  
TGTTTTTGGTGGCATGAGGACAAAATTTCAATTGAAGGTAAGATAAGAATAAAAACTATGTT  
TAC

SEQ ID NO: 9\_AA210825\_H

CACGAGGGCTACTGGCGCCTGGCGACCCTCCCTGCCCCCACCACACCCCGCTCCGGCAA  
CGCCCCCTTCCTCACGGCTCCCGACCGAACTTTTCTCCAACCTTCTGCGACTCGTGAGATT  
CCCTTCTACCCACTCCGGCCCTCGGGACCCCTCTGCCCATCCCTTGGCCGGTCCGGTCCC  
TGCGAACCCCTTTATCTCTGGAATCCACTCGGTCCCCGACTCAGAGACTCCTGCCCTCCA  
CCCCCAAGGACCCCGCCATCCTCAGGTCCCTCCGCCTGCCAGATCTTTTCTCGGATCCC  
CGCTCTCCACACCTGCTCACGAGATCCCGCGGATCTAGAACCAGGGTCCCCCGGGGC  
CCCCCGGCGGGTCCCGGGTGGGCTCCAGGCGGGCGGTCCCCGGCCTCCCCCATGGCCAC  
CGCCCCCTCATTATCCCGCCGGGCTCCCTGGCTCTCCCGGGCGGGGTCTCCTCCGCCCC  
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CCAACCTCCTGCAGCTGGTGCCTCGTCCGGAGACATCCAGGAGGGCGACCTGGTGGAGG  
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TGCGCCAGGGCCTCAAGTGCGATGGCTGCGGGCTGAACTACCACAAGCGCTGTGCCTTCA  
GCATCCCCAACAACCTGTAGTGGGGCCCGCAAACGGCGCCTGTCATCCACGTCTCTGGCCA  
GTGGCCACTCGGTGCGCCTCGGCACCTCCGAGTCCCTGCCCTGCACGGCTGAAGAGCTGA  
GCCGTAGCACCACCGAACTCCTGCCTCGCCGTCCCCCGTCATCCTCTTCCTCCTCTTCTG  
CCTCATCGTATACGGGCGGCCCATTTAGAGCTGGACAAGATGCTGCTCTCCAAGGTCAAGG  
TGCCGCACACCTTCTCATCCACAGCTATACACGGCCACCGTTTGCCAGGCTTGCAAGA  
AACTCCTCAAGGGCCTCTTCCGGCAGGGCCTGCAATGCAAAGACTGCAAGTTTAACTGTC

## FIGURE 2H

ACAAACGCTGCGCCACCCGCGTCCCTAATGACTGCCTGGGGGAGGCCCTTATCAATGGAG  
ATGTGCCGATGGAGGAGGCCACCGATTTGAGCGAGGCTGACAAGAGCGCCCTCATGGATG  
AGTCAGAGGACTCCGGTGTTCATCCCTGGCTCCCACTCAGAGAATGCGCTCCACGCCAGTG  
AGGAGGAGGAAGGCGAGGGGAGGCAAGGCCAGAGCTCCCTGGGGTACATCCCCCTAATGA  
GGGTGGTGCAATCGGTGCGACACACGACGCGGAAATCCAGCACCCACGCTGCGGGGAGGGTT  
GGGTGGTTCATTACAGCAACAAGGACACGCTGAGAAAGCGGCACTATTGGCGCCTGGACT  
GCAAGTGTATCACGCTCTTCCAGAACAACACGACCAACAGATACTATAAGGAAATTCCGC  
TGTCAGAAATCCTCACGGTGGAGTCCGCCCAGAACTTCAGCCTTGTGCCGCCGGGCACCA  
ACCCACACTGCTTTGAGATCGTCACTGCCAATGCCACCTACTTCGTGGGCGAGATGCCTG  
GCGGGACTCCGGGTGGGCCAAGTGGGCAGGGGGCTGAGGCCGCCCGGGGGCTGGNNGAGA  
CAGCCATCCGCCAGGCCCTGATGCCCCGTCATCCTTCAGGACGCACCCAGCGCCCCAGGCC  
ACGCGCCCCACAGACAAGCTTCTCTGAGCATCTCTGTGTCCAACAGTCAGATCCAAGAGA  
ATGTGGACATTGCCACTGTCTACCAGATCTTCCCTGACGAAGTGCTGGGCTCAGGGCAGT  
TTGGAGTGGTCTATGGAGGAAAACACCGGAAGACAGGCCGGGACGTGGCAGTTAAGGTCA  
TTGACAAACTGCGCTTCCCTACCAAGCAGGAGAGCCAGCTCCGGAATGAAGTGGCCATTC  
TGCAGAGCCTGCGGCATCCCGGGATCGTGAACCTGGAGTGCATGTTTCGAGACGCCTGAGA  
AAGTGTTTGTGGTGATGGAGAAGCTGCATGGGGACATGTTGGAGATGATCCTGTCCAGTG  
AGAAGGGCCGGCTGCCTGAGCGCCTCACCAAGTTCCTCATCACCCAGATCCTGGTGGCTT  
TGAGACACCTTCACTTCAAGAACATTGTCCACTGTGACTTGAAACCAGAAAACGTGTTGC  
TGGCATCAGCAGACCCATTTCCCTCAGGTGAAGCTGTGTGACTTTGGCTTTGCTCGCATCA  
TCGGCGAGAAGTCGTTCCGCCGCTCAGTGGTGGGCACGCCGGCCTACCTGGCACCCGAGG  
TGCTGCTCAACCAGGGCTACAACCGCTCGCTGGACATGTGGTCAGTGGGCGTGATCATGT  
ACGTCAGCCTCAGCGGCACCTTCCCTTTCAACGAGGATGAGGACATCAATGACCAGATCC  
AGAACGCCGCCTTCATGTACCCGGCCAGCCCCCTGGAGCCACATCTCAGCTGGAGCCATTG  
ACCTCATCAACAACCTGCTGCAGGTGAAGATGCGCAAACGCTACAGCGTGGAACAAATCTC  
TCAGCCACCCCTGGTTACAGGAGTACCAGACGTGGCTGGACCTCCGAGAGCTGGAGGGGA  
AGATGGGAGAGCGATACATCACGCATGAGAGTGACGACGCGCGCTGGGAGCAGTTTGCAG  
CAGAGCATCCGCTGCCTGGGTCTGGGCTGCCACCGGACAGGGATCTCGGTGGGGCCTGTC  
CACACAGGACCACGACATGCAGGGGCTGGCGGAGCGCATCAGTGTTCTCTGAGGTCCTG  
TGCCCTCGTCCAGCTGCTGCCCTCCACAGCGGTTCTTCACAGGATCCCAGCAATGAACTG  
TTCTAGGGAAAGTGGCTTCCCTGCCCAAACCTGGATGGGACACGTGGGGAGTGGGGTGGGGG  
GAGCTATTTCCAAGGCCCTCCCTGTTTCCCCAGCAATTAAACGGACTCATCTCTGGCC  
CCATGGCCTTGATCTCAGCAAAA

SEQ ID NO: 10\_AA127299\_H

ATTCAATTCATAATTGTTGGTGCAAAAGATTTGCTTGCTATGGATTCAAATGGTCTTTCT  
GATCCTTACATCAAAATCACAAATCTTTCTCAAAAACGAAAGTGATTAAAGAAAACCTTTG  
ACTCCAACCTTGGAATGAACTTTTTTTGTGCATTTTCCAGAAAAACAACCCCTTGAATTA  
GAATGTTGGGACCACGATACTTTTTCAGATGATTTTATTGGCAAGGCTTCCATTTCTTTG  
GCAGAGATTCCAGCTTTGGCAGAAGTTGATATGTGGATAGATATGAAAACGAAAAAAGGA  
GAATTTGCAGGAAAA

SEQ ID NO: 11\_AA316804\_H

ATGTCTGCAAATAATTCCCCTCCATCAGCCCAGAAGTCTGTATTACCCACAGCTATTCCCT  
GCTGTGCTTCCAGCTGCTTCTCCGTGTTCAAGTCCTAAGACGGGACTCTCTGCCCGACTC  
TCTAATGGAAGCTTCAGTGCACCATCACTACCAACTCCAGAGGCTCAGTGCATACAGTT  
TCATTTCTACTGCAAATTGGCCTCACACGGGAGAGTGTTACCATTTGAAGCCCAGGAACTG  
TCTTTATCTGCTGTCAAGGATCTTGTGTGCTCCATAGTTTATCAAAAGTTTCCAGAGTGT  
GGATTCTTTGGCATGTATGACAAAATTCTTCTCTTTCGCCATGACATGAACTCAGAAAAC  
ATTTTGCAGCTGATTACCTCAGCAGATGAAATACATGAAGGAGACCTAGTGGAAGTGGTT

## FIGURE 21

CTTTCAGCTTTAGCCACAGTAGAAGACTTCCAGATTTCGTCCACATACTCTCTATGTACAT  
TCTTACAAAGCTCCTACTTTCTGTGATTACTGTGGTGAGATGCTGTGGGGATTGGTACGT  
CAAGGACTGAAATGTGAAGGCTGTGGATTAAATTACCATAAACGATGTGCCTTCAAGATT  
CCAAATAACTGTAGTGGAGTAAGAAAGAGACGTCTGTCAAATGTATCTTTACCAGGACCC  
GGCCTCTCAGTTCCAAGACCCCTACAGCCTGAATATGTAGCCCTTCCCAGTGAAGAGTCA  
CATGTCCACCAGGAACCAAGTAAGAGAATTCTTCTTGGAGTGGTCGCCCCAATCTGGATG  
GAAAAGATGGTAATGTGCAGAGTGAAAGTTCCACACACATTTGCTGTTCACTCTTACACC  
CGTCCCACGATATGTCAGTACTGCAAGCGGTTACTGAAAGGCCTCTTTTCGCCAAGGAATG  
CAGTGTAAGATTGCAAATTCAACTGCCATAAACGCTGTGCATCAAAAGTACCAAGAGAC  
TGCCTTGGAGAGGTTACTTTCAATGGAGAACCCTTCCAGTCTGGGAACAGATACAGATATA  
CCAATGGATATTGACAATAATGACATAAATAGTGATAGTAGTCGGGGTTTGGATGACACA  
GAAGAGCCATCACCCCCAGAAGATAAGATGTTCTTCTTGGATCCATCTGATCTCGATGTG  
GAAAGAGATGAAGAAGCCGTTAAAACAATCAGTCCATCAACAAGCAATAATATTCCGCTA  
ATGAGGGTGTACAATCCATCAAGCACACAAAGAGGAAGAGCAGCACAAATGGTGAAGGAA  
GGGTGGATGGTCCATTACACCAGCAGGGATAACCTGAGAAAGAGGCATTATTGGAGACTT  
GACAGCAAATGTCTAACATTATTTTCAGAATGAATCTGGATCAAAGTATTATAAGGAAATT  
CCTCTTTCAGAAATTCTCCGCATATCTTCACCACGAGATTTACAAACATTTACAAAGGC  
AGCAATCCACACTGTTTTGAAATCATTACTGATACTATGGTATACTTCGTTGGTGAGAAC  
AATGGGGACAGCTCTCATAATCCTGTTCTTGCTGCCACTGGAGTTGGACTTGATGTAGCA  
CAGAGCTGGGAAAAAGCAATTCGCCAAGCCCTCATGCCTGTTACTCCTCAAGCAAGTGTT  
TGCCTTCTCCAGGGCAAGGGAAAGATCACAAAGATTTGTCTACAAGTATCTCTGTATCT  
AATTGTCAGATTCAGGAGAATGTGGATATCAGTACTGTTTACCAGATCTTTGCAGATGAG  
GTGCTTGGTTCAGGCCAGTTTGGCATCGTTTATGGAGGAAAACATAGAAAGACTGGGAGG  
GATGTGGCTATTAAAGTAATTGATAAGATGAGATTCCCCACAAAACAAGAAAGTCACTC  
CGTAATGAAGTGGCTATTTTACAGAATTTGCACCATCCTGGGATTGTAAACCTGGAATGT  
ATGTTTGAACCCCGAAGCAGTCTTTGTAGTAATGGAAAAGCTGCATGGAGATATGTTG  
GAAATGATTCTATCCAGTGAGAAAAGTCGGCTTCCAGAACGAATTACTAAATTCATGGTC  
ACACAGATACTTGTTGCTTTGAGGAATCTGCATTTTAAGAATATTGTGCACTGTGATTTA  
AAGCCAGAAAATGTGCTGCTTGCATCAGCAGAGCCATTTCTCAGGTGAAGCTGTGTGAC  
TTTGGATTTGCACGCATCATTGGTGAAAAGTCATTTCAGGAGATCTGTGGTAGGAACCTCA  
GCATACTTAGCCCCCTGAAGTTCTCCGGAGCAAAGGTTACAACCGTTCCCTAGATATGTGG  
TCAGTGGGAGTTATCATCTATGTGAGCCTCAGTGGCACATTTCTTTTAAATGAGGATGAA  
GATATAAATGACCAAATCCAAAATGCTGCATTTATGTACCCACCAAATCCATGGAGAGAA  
ATTTCTGGTGAAGCAATTGATCTGATAAACAATCTGCTTCAAGTGAAATGAGAAAACGT  
TACAGTGTTGACAAATCTCTTAGTCATCCCTGGCTACAGGACTATCAGACTTGGCTTGAC  
CTTAGAGAATTTGAAACTCGCATTGGAGAACGTTACATTACACATGAAAGTGATGATGCT  
CGCTGGGAAATACATGCATACACACATAACCTTGTATACCCAAAGCACTTCATTATGGCT  
CCTAATCCAGATGATATGGAAGAAGATCCTTAA

SEQ ID NO: 12\_PKNBETA\_H

ATGGAGGAGGGGGCGCCGCGGCAGCCTGGGCGGAGCCAGTGGCCCCCAGAGGATGAGAAG  
GAGGTGATCCGCCGGGCCATCCAGAAAGAGCTGAAGATCAAGGAGGGGGTGGAGAACCCTG  
CGGCGCGTGGCCACAGACCGCCGCACTTGGGCCATGTGCAGCAGCTGCTGCGGTCTCTCC  
AACCGCCGCTGGAGCAGCTGCATGGCGAGCTGCGGGAGCTGCACGCCCGAATCCTGCTG  
CCCGGCCCTGGGCCTGGCCCAGCTGAGCCTGTGGCCTCAGGACCCCGGCCGTGGGCAGAG  
CAGCTCAGGGCTCGGCACCTAGAGGCTCTCCGGAGGCAGCTGCATGTGGAGCTGAAGGTG  
AAACAGGGGGCTGAGAACATGACCCACACGTGCGCCAGTGGCACCCCCAAGGAGAGGAAG  
CTCCTTGCAGCTGCCCAGCAGATGCTGCGGGACAGCCAGCTGAAGGTGGCCCTGCTGCGG  
ATGAAGATCAGCAGCCTGGAGGCCAGTGGGTCCCCGGAGCCAGGGCCTGAGCTACTGGCG  
GAGGAGCTACAGCATCGACTGCACGTTGAGGCAGCGGTGGCTGAGGGCGCCAAGAACGTG

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FIGURE 2J

CTGAAACTGCTTAGTAGCCGAGAGAACACAGGACCGCAAGGCACTGGCTGAGGCCAGGCC  
CAGCTACAGGAGTCTCTCAGAAACTGGACCTCCTGCGCTTGGGCTTGGAGCAGCTGCTG  
GAGCAACTGCCTCCTGCCCCACCTTTGCGCAGCAGAGTGACCCGAGAGTTGCGGGCTGCG  
GTGCTTGGATAACCCCCAGCCTTCAGGGACACCTGTGAAGCCCCACCGCCCTAACAGGGACA  
CTGCAGGTCCGCTCCTGGGCTGTGAACAGTTGCTGACAGCCGTGCCTGGGCGCTCCCCA  
GCGGCCGCACTGGCCAGCAGCCCCCTCCGAGGGCTGGCTTCGGACCAAGGCCAAGCACCAG  
CGTGGCCGAGGCGAGCTTGCCAGTGAGGTGCTGGCTGTGCTAAAGGTGGACAACCGTGTT  
GTGGGGCAGACGGGCTGGGGGCAGGTGGCCGAACAGTCCTGGGACCAGACCTTTGTCATC  
CCACTGGAGCGAGCCCGTGAGCTGGAGATTGGGGTACACTGGCGGGACTGGCGGCAGCTA  
TGTGGCGTGGCCTTCCTGAGACTTGAAGACTTCCTGGACAATGCCTGTCACCAACTGTCC  
CTCAGCCTGGTACCGCAGGGACTGCTTTTTGCCCAGGTGACCTTCTGCGATCCTGTCATT  
GAGAGGCGGCCCCGGCTGCAGAGGCAGGAACGCATCTTCTCTAAACGCAGAGGCCAGGAC  
TTCCTGAGGCGTTCGCAGATGAACCTCGGCATGGCGGCCTGGGGGCGCCTCGTCATGAAC  
CTGCTGCCCCCTGCAGCTCCCCGAGCACAATCAGCCCCCTAAAGGATGCCCTCGGACC  
CCAACAACACTGCGAGAGGCCTCTGACCCTGCCACTCCCAGTAATTTCTGCCCCAAGAAG  
ACCCCTTGGGTGAAGAGATGACACCCCCACCCAAGCCCCCACGCCTCTACCTCCCCCAG  
GAGCCAACATCCGAGGAGACTCCGCGCACCAACGTCCTCCCATATGGAGCCTAGGACTCGA  
CGTGGGCCATCTCCACCAGCCTCCCCCACCAGGAAACCCCTCGGCTTCAGGACTTCCGC  
TGCTTAGCTGTGCTGGGCCGGGACACTTTGGGAAGGTCCTCCTGGTCCAGTTCAAGGGG  
ACAGGGAAATACTACGCCATCAAAGCACTGAAGAAGCAGGAGGTGCTCAGCCGGGACGAG  
ATAGAGAGCCTGTACTGCGAGAAGCGGATCCTGGAGGCTGTGGGCTGCACAGGGGCACCCT  
TTCCTGCTCTCCCTCCTTGTCTGCTTCCAGACCTCCAGCCATGCCCGCTTTGTGACTGAG  
TTTGTGCCTGGTGGTGACCTCATGATGCAGATCCACGAGGATGTCTTCCCCGAGCCCCAG  
GCCCCGCTTCTACGTGGCTTGTGTTGTCTGGGGCTGCAGTTCTTACACGAGAAGAAGATC  
ATTTACAGGGACCTGAAGTTGGATAACCTTCTGCTGGATGCCCAGGGATTCTTGAAGATC  
GCAGACTTTGGACTCTGCAAGGAAGGGATCGGCTTCGGGGACCGGACTAGCACCTTCTGT  
GGCACCCCGGAGTTCTTGGCTCCCGAGGTGCTGACCCAGGAGGCATACACACAGGCCGTC  
GACTGGTGGGCGCTGGGTGTGCTGCTCTACGAGATGCTGGTGGGTGAGTGCCCGTTCCCA  
GGGGACACAGAGGAAGAGGTGTTTGAAGTGCATCGTCAACATGGACGCCCCCTACCCCGGC  
TTTCTGTCGGTGCAAGGGCTTGAGTTCATTCAGAAGCTCCTCCAGAAGTGCCCGGAGAAG  
CGCCTCGGGGCAGGTGAGCAGGATGCCGAGGAGATCAAGGTCCAGCCATTCTTCAGGACC  
ACCAACTGGCAAGCCCTGCTCGCCCGCACCATCCAGCCCCCTTCGTGCCTACCCTGTGT  
GGCCCTGCGGACCTGCGCTACTTTGAGGGCGAGTTCACAGGGCTGCCGCCTGCCCTGACC  
CCACCTGCACCCACAGCCTCCTCACTGCCCGCCAACAGGCCGCTTCCGGGACTTCGAC  
TTTGTGTCAGAGCGATTCTTGAACCTGA

SEQ ID NO: 13\_AI021023\_M\_PKNBETA\_M

GCTGAAGTGGGATAACCTTCTGCTGGATGCCCAGGGATTCTTGAAGATCGCAGACTTTGG  
ACTCTGCAAGGAAGGGATCGGCTTCGGGGACCGGACTAGCACCTTCTGTGGCACCCCGGA  
GTTCTTGGCTCCCGAGGTGCTGACCCAGGAGGCATACACACGGGCTGTGGACTGGTGGGG  
GCTGGGTGTGCTGCTCTACGAGATGCTGGTGGGTGAGTGCCCGTTCCAGGGGGACACAGA  
GGAAGAGGTGTTTGAAGTGCATCGTCAACATGGACGCCCCCTACCCCGGCTTTCTGTGGT  
GCAAGGGCTTGAGTTCATTCAGAAGCTCCTCCAGAAGTGCCCGGAGAAGCGCCTCGGGGC  
GGGTGAGCAGGATGCCGAGGAGATCAAGGTCCAGCCATTCTTCAGGACCACCAACTGGCA  
AGCCCTGCTCGCCCGCACCATCCAGCCCCCTTTGTGCTTACCCTGTGTGGCCCTGCGGA  
CCTGCGCTACTTTGAGGGCGAGTTCACAGGGCTGCCGCCTGCCCTGACCCACCTGCACC  
CCACAGCCTCCTCACTGCCCGCCAACAGGCCGCTTCCGGGACTTCGACTTTGTGTCAGA  
GCGATTCTTGAACCTGAGGGCATCTCCTGGCACCTCTGTCCCCTTCCCCCACAGACTG  
TTAGAGCCTCTGCTCGTTACCCCGTGCGCCCTGCCTGGAGGTCCAGGCCTTGCTGGGTAC  
TTCTGAGCCCTTGGGATTCAAAGTGGCAGCCATGGGGCCACTGTTGTGGGCTTTGCTCAG

## FIGURE 2K

TGTCACTGGGCAAAGTGTGTCCCTTCCCCCTCCAGCTCGCCCTCTTCTACCTCCCAGCGA  
GACCTGGCCCAGAAAGGGTGCCGCAGCAAGGAGTGATATGGTTTGTCTTTTAAAGACTGG  
ACTTGCTTTATATTAAATTTGTAAAAGTG

SEQ ID NO: 14\_H19102\_H

GGTGGCAACATCCGGGGTCCCTGGGCCCCGAGGCTGGAAGAGCCTCTGGACAGGTTTGGGA  
ACCATCAGGTCAGATCTGGAAGAACTCTGGGAACTACGGGGGCACCACTATCTGCACCAG  
GAATCCCTAAAGCCAGCCCCAGTACTGGTAGAGAAGCCTCTGCCAGAGTGGCCAGTGCCT  
CAGTTCATCAACCTCTTTCTACCAGAGTTTCCCATTAGGCCCCATTAGGGGGCAGCAGCAG  
CTGAAGATTTTAGGCCTCGTGGCTAAAGGCTCCTTTGGAAGTGTCTCAAGGTGCTAGAT  
TGCACCCAGAAAGCTGTATTTGCAGTGAAGGTGGTGCCCAAGGTAAAGGTCCTACAGAGG  
GATACCGTGAGGCAGTGCAAAGAGGAGGTTAGCATCCAGCGACAGATCAACCATCCCTTT  
GTACACAGCTTGGGGGACAGCTGGCAGGGAAAACGGCACCTTTTCATTATGTGTAGCTAC  
TGCAGCACAGATCTGTACTCCCTTTGGTCCGGCTGTTGGCTGCTTTTCTGAGGCTTCCATC  
CGTCTCTTTGCTGCCGAGTTGGTGCTGGTACTGTGTTATCTCCATGACTTGGGCATCATG  
CATCGAGATGTGAAGATGGAGAATATTCTTCTAGATGAACGAGGCCATCTGAAACTGACA  
GACTTTGGTCTGTCCCGCCACGTGCCCCAGGGAGCTCAAGCCTACACTATCTGTGGCACT  
CTTCAGTACATGGCCCCAGAGGTCCTAAGTGGAGGACCTTACAACCATGCTGCTGATTGG  
TGGTCCCTGGGTGTCTTGCTTTTCTCTCTGGCGACTGGAAAGTTTCCAGTGGCTGCAGAG  
AGAGATCATGTGGCCATGTTGGCAAGTGTGACCCACAGTGAATCTGAGATCCCAGCTTCT  
CTTAACCAGGGCCTCTCACTCCTGCTCCATGAGCTCTTATGCCAGAACCCCTCCATCGT  
CTACGTTATCTGCATCACTTCCAGGTCCACCCTTTCTTTTCGGGGTGTGGCCTTCGACCCA  
GAGCTCCTACAGAAGCAGCCAGTGAATTTGTACGGAGACACAAGCTACCCAGCCCAGT  
TCAGCGGAGACCATGCCCTTTGACGACTTTGACTGTGATCTGGAGTCCTTCTTGCTCTAC  
CCTATCCCTGCTTGA

SEQ ID NO: 15\_AA476563\_H

ATGGAATTCTTTAGGATAGACAGTAAGGATAGCGCAAGTGAACTCCTGGGACTTGACTTT  
GGAGAAAAATTGTATAGTCTAAAATCAGAACCTTTGAAACCATTTCTTTACTCTTCCAGAT  
GGAGACAGTGCTTCTAGGAGTTTTAATACTAGTGAAAGCAAGGTAGAGTTTAAAGCTCAG  
GACACCATTAGCAGGGGCTCAGATGACTCAGTGCCAGTTATTTTCGTTTAAAGATGCTGCT  
TTTGATGATGTCAGTGGTACTGATGAAGGAAGACCTGATCTTCTTGTAATTTACCTGGT  
GAATTGGAGTCAACAAGAGAAGCTGCAGCAATGGGACCTACTAAGTTTACACAACTAAT  
ATAGGGATAATAGAAAATAAACTCTTGGAAGCCCCTGATGTTTTATGCTCAGGCTTAGT  
ACTGAACAATGCCAAGCACATGAGGAGAAAGGCATAGAGGAACTGAGTGATCCCTCTGGG  
CCCAAATCCTATAGTATAACAGAGAAACACTATGCACAGGAGGATCCCAGGATGTTATTT  
GTAGCAGCTGTTGATCATAGTAGTTCAGGAGATATGTCTTTGTTACCCAGCTCAGATCCT  
AAGTTTCAAGGACTTGGAGTGGTTGAGTCAGCAGTAACTGCAAACAACACAGAAGAAAGC  
TTATTCCGTATTTGTAGTCCACTCTCAGGTGCTAATGAATATATTGCAAGCACAGACACT  
TTAAAAACAGAAGAAGTATTGCTGTTTACAGATCAGACTGATGATTTGGCTAAAGAGGAA  
CCAACCTTCTTTATTCCAGAGAGACTCTGAGACTAAGGGTGAAAGTGGTTTAGTGCTAGAA  
GGAGACAAGGAAATACATCAGATTTTTTGAGGACCTTGATAAAAAATTAGCACTAGCCTCC  
AGGTTTTTACATCCCAGAGGGCTGCATTCAAAGATGGGCAGCTGAAATGGTGGTAGCCCTT  
GATGCTTTACATAGAGAGGGAATTGTGTGCCGCGATTTGAACCCAAACAACATCTTATTG  
AATGATAGAGGACACATTCAGCTAACGTATTTTAGCAGGTGGAGTGAGGTTGAAGATTCC  
TGTGACAGCGATGCCATAGAGAGAATGTACTGTGCCCCAGAGGTTGGAGCAATCACTGAA  
GAACTGAAGCCTGTGATTGGTGGAGTTTGGGTGCTGTCCTCTTTGAACTTCTCACTGGC  
AAGACTCTGGTTGAATGCCATCCAGCAGGAATAAATACTCACACTACTTTGAACATGCCA  
GAATGTGTCTCTGAAGAGGCTCGCTCACTCATTCAACAGCTCTTGCAAGTTCAATCCTCTG



## FIGURE 2L

GAACGACTTGGTGCTGAGTTGCTGGTGTGAAGATATCAAATCTCATCCATTTTTTTACC  
CCTGTGGATTGGGCAGAACTGATGAGATGA

SEQ ID NO: 16\_AA626690\_H

ATGCTACCATTCGCTCCTCAGGACGAGCCCTGGGACCGAGAAATGGAAGTGTTTCAGCGGC  
GGCGGCGCGAGCAGCGGCGAGGTAAATGGTCTTAAAATGGTTGATGAGCCAATGGAAGAG  
GGAGAAGCAGATTCTTGTCATGATGAAGGAGTTGTTAAAGAAATCCCTATTACTCATCAT  
GTTAAGGAAGGCTATGAGAAAGCAGATCCTGCACAGTTTGAGTTGCTCAAGGTTCTTGGT  
CAGGGGTCATTTGGAAAGGTTTTCTTGTTAGAAAGAAGACCGGTCCTGATGCTGGGCAG  
CTCTATGCAATGAAGGTGTTAAAAAAGCCTCTTTAAAAGTTTCGAGACAGAGTTCGGACA  
AAGATGGAGAGGGATATACTGGTGGAAAGTAAATCATCCATTTATTGTCAAATTGCACTAT  
GCCTTTCAGACTGAAGGGAAACTGTACTTAATACTGGATTTTCTCAGGGGAGGAGATGTT  
TTCACAAGATTATCCAAAGAGGTTCTGTTTACAGAGGAAGATGTGAAATTCTACCTCGCA  
GAACTGGCCCTTGCTTTGGATCATCTGCACCAATTAGGAATTGTTTATAGAGACCTGAAG  
CCAGAAAACATTTTGCTTGATGAAATAGGACATATCAAATTAACAGATTTTGGACTCAGC  
AAGGAGTCAGTAGATCAAGAAAAGAAGGCTTACTCATTTTGTGGTACAGTAGAGTATATG  
GCTCCTGAAGTAGTAAATAGGAGAGGCCATTCCCAGAGTGCTGATTGGTGGTCATATGGT  
GTTCTTATGTTTGAAATGCTTACTGGTACTCTGCCATTTCAAGGTAAAGACAGAAATGAG  
ACCATGAATATGATATTAAAAGCAAAACTTGGAATGCCTCAATTTCTTAGTGCTGAAGCA  
CAAAGTCTTCTAAGGATGTTATTCAAAGGAATCCAGCAAATAGATTGGGATCAGAAGGA  
GTTGAAGAAATCAAAGACATCTGTTTTTTGCAAATATTGACTGGGATAAATTATATAAA  
AGAGAAGTTCAACCTCCTTTCAAACCTGCTTCTGGAAAACCAGATGATACTTTTTTGTTTT  
GATCCTGAATTTACTGCAAAAACACCTAAAGATTCTCCCGGTTTGCCAGCCAGTGCAAAT  
GCTCATCAGCTCTTCAAAGGATTCAGCTTTGTTGCAACTTCTATTGCAGAAGAATATAAA  
ATCACTCCTATCACAAGTGCAAATGTATTACCAATTGTTTCAGATAAATGGAAATGCTGCA  
CAATTTGGTGAAGTATATGAATTGAAGGAGGATATTGGTGTGGCTCCTACTCTGTTTGC  
AAGCGATGCATACATGCAACTACCAACATGGAATTTGCAGTGAAGATCATTGACAAAAGT  
AAGCGAGACCCTTCAGAAGAGATTGAAATATTGATGCGCTATGGACAACATCCCAACATT  
ATTACTTTGAAGGATGTCTTTGATGATGGTAGATATGTTTACCTTGTTACGGATTTAATG  
AAAGGAGGAGAGTTACTTGACCGTATTCTCAAACAAAAATGTTTCTCGGAACGGGAGGCT  
AGTGATATACTATATGTAATAAGTAAGACAGTTGACTATCTTCATTGTCAAGGAGTTGTT  
CATCGTGATCTTAAACCTAGTAATATTTTATACATGGATGAATCAGCCAGTGCAAGATTCA  
ATCAGGATATGTGATTTTGGGTTTGCAAAACAACCTTCGAGGAGAAAATGGACTTCTCTTA  
ACTCCATGCTACACTGCAAACCTTTGTTGCACCTGAGGTTCTTATGCAACAGGGATATGAT  
GCTGCTTGTGATATCTGGAGTTTAGGAGTCCTTTTTTACACAATGTTGGCTGGCTACACT  
CCATTTGCTAATGGCCCCAATGATACTCCTGAAGAGATACTGCTGCGTATAGGCAATGGA  
AAATTCTCTTTGAGTGGTGGAACTGGGACAATATTCAGACGGAGCAAAGGATTTGCTT  
TCCCATATGCTTCATATGGACCCACATCAGCGGTATACTGCTGAACAAATATTAAAGCAC  
TCATGGATAACTCACAGAGACCAGTTGCCAAATGATCAGCCAAAGAGAAATGATGTGTCA  
CATGTTGTTAAGGGAGCAATGGTTGCAACATACTCTGCCCTGACTCACAAGACCTTTCAA  
CCAGTCCTAGAGCCTGTAGCTGCTTCAAGCTTAGCCCAGCGACGGAGCATGAAAAAGCGA  
ACATCAACTGGCCTGTAA

SEQ ID NO: 17\_AA215680\_H

ATGAGCCTGGTGGCCTGTGAGTGCCTGCCCAGCCCCGGCCTGGAGCCTGAGCCTTGCTCA  
CGAGCACGGTCCCAAGCTCACGTGTACCTGGAGCAGATTCGCAACAGGGTGGCTCTGGGA  
GTGCCTGACATGACAAAACGTGACTATCTGGTGGATGCGGCCACGCAGATCCGGCTGGCC  
CTGGAGCGCGATGTTAGTGAGGACTATGAGGCGGCCTTCAACCACTATCAGAATGGCGTG  
GACGTGCTGCTCCGTGGCATAACGTTGACCCCAACAAGGAGCGACGTGAGGCTGTGAAG  
CTGAAAATTACCAAATACCTGCGGCGGGCAGAGGAGATCTTCAACTGCCACCTGCAGCGG

## FIGURE 2M

CCGCTGAGCAGTGGAGCCAGCCCCAGCGCGGGTTTCAGCAGCCTGAGGCTCCGGCCCCATT  
CGCACGCTGAGCTCTGCCGTGGAGCAGCTGAGGGGCTGCAGGGTGGTCGGGGTCATCGAG  
AAGGTGCAGCTGGTCCAGGACCCGGCAACCGGAGGGACCTTTGTGGTGAAGAGCCTACCC  
AGGTGCCACATGGTGAGCAGGGAGCGGCTGACCATCATCCCCACAGGAGTCCCCCTACATG  
ACGAAGCTGCTCAGGTACTTTGTGAGCGAGGACTCCATCTTCCTGCACCTGGAGCATGTS  
CAAGGAGGCACTCTCTGGTCCCACCTGCTCTCCCAGGCGCACTCCCGACATTCTGGGCTC  
AGCTCTGGCTCTACCCAGGAGAGGATGAAGGCTCAGCTCAACCCCCACCTCAACCTCCTG  
ACCCCAGCGAGGCTTCCCTCAGGCCATGCCCTGGCCAGGACAGAATCGCCCTGGAGCCT  
CCTAGGACTTCTCCGAACCTTCTCCTAGCTGGGGAGGCCCCATCCACCAGACCCCAGAGG  
GAGGCTGAAGGTGAACCCACAGCCAGGACCAGCACCTCTGGCTCCTCGGACCTTCCAAAG  
GCCCCAGGTGGCCACCTGCACCTTCAAGCTAGGAGGGCTGGCCAGAACTCAGACGCTGGG  
CCCCCTCGGGGGCTCACTTGGGTTCCTGAGGGGGCCGGCCCCGGTGCTAGGGGGCTGTGGC  
CGAGGCATGGATCAGAGCTGCCTGTCAGCAGATGGGGCCGGCCGGGGCTGTGGCAGGGCC  
ACCTGGAGTGTGAGAGAGGAGCAGGTGAAGCAGTGGGCGGCAGAGATGCTGGTAGCGCTG  
GAGGCGCTGCACGAGCAGGGGGTGCTGTGCCGGGACCTCCACCCCCGGGAACCTGCTCCTG  
GACCAGGCAGGTCACATCCGGCTCACATATTTTGGCCAGTGGTCAGAGGTGGAGCCCCAG  
TGCTGCGGGGAGGCCGTGGACAATCTCTACAGCGCCCCAGAGGTGGGTGGGATTTCCGAG  
CTGACGGAAGCCTGTGACTGGTGGAGCTTTGGGTCTCTACTGTATGAACTGCTGACGGGA  
ATGGCACTGTCCCAGAGCCACCCTTCAGGAATCCAGGCCACACCCAGCTCCAGCTGCCC  
GAGTGGCTCAGTCGCCCAGCGGCTCTCTGCTGACTGAGCTGCTGCAGTTCGAGCCTACC  
CGGCGCCTGGGCATGGGAGAAGGTGGTGTGAGCAAACTCAAGTCCCATCCCTTTTTTCAGT  
ACCATCCAATGGAGCAAGCTGGTGGGGTAA

SEQ ID NO: 18\_SGK\_H

ATGACGGTGAAAACCTGAGGCTGCTAAGGGCACCCCTCACTTACTCCAGGATGAGGGGCATG  
GTGGCAATTCTCATCGCTTTCATGAAGCAGAGGAGGATGGGTCTGAACGACTTTATTCAG  
AAGATTGCCAATAACTCCTATGCATGCAAACACCCTGAAGTTCAGTCCATCTTGAAGATC  
TCCCAACCTCAGGAGCCTGAGCTTATGAATGCCAACCCTTCTCCTCCACCAAGTCCTTCT  
CAGCAAATCAACCTTGGCCCCGTCGTCCAATCCTCATGCTAAACCATCTGACTTTCCTTC  
TTGAAAGTGATCGGAAAGGGCAGTTTTTGGAAAGGTTCTTCTAGCAAGACACAAGGCAGAA  
GAAGTGTCTATGCAGTCAAAGTTTTACAGAAGAAAGCAATCCTGAAAAAGAAAGAGGAG  
AAGCATATTATGTGCGAGCGGAATGTTCTGTTGAAGAATGTGAAGCACCCCTTTCCTGGTG  
GGCCTTCACTTCTCTTTCCAGACTGCTGACAAATTGTACTTTGTCTTAGACTACATTAAT  
GGTGGAGAGTTGTTCTACCATCTCCAGAGGGAACGCTGCTTCCCTGGAACACGGGCTCGT  
TTCTATGCTGCTGAAATAGCCAGTGCCTTGGGCTACCTGCATTCACTGAACATCGTTTAT  
AGAGACTTAAAACCAGAGAATATTTTGTAGATTACAGGGACACATTGTCCTTACTGAT  
TTCGGACTCTGCAAGGAGAACATTGAACACAACAGCACAAACATCCACCTTCTGTGGCACG  
CCGGAGTATCTCGCACCTGAGGTGCTTCATAAGCAGCCTTATGACAGGACTGTGGACTGG  
TGGTGCCTGGGAGCTGTCTTGTATGAGATGCTGTATGGCCTGCCGCCTTTTTATAGCCGA  
AACACAGCTGAAATGTACGACAACATTCTGAACAAGCCTCTCCAGCTGAAACCAAATATT  
ACAAATTCCGCAAGACACCTCCTGGAGGGCCTCCTGCAGAAGGACAGGACAAAGCGGCTC  
GGGGCCAAGGATGACTTCATGGAGATTAAGAGTCATGTCTTCTTCTCCTTAATTAAGTGG  
GATGATCTCATTAATAAGAAGATTACTCCCCCTTTTAACCCAAATGTGAGTGGGCCCCAAC  
GAGCTACGGCACTTTGACCCCCGAGTTTACCGAAGAGCCTGTCCCCAACTCCATTGGCAAG  
TCCCCTGACAGCGTCCTCGTCACAGCCAGCGTCAAGGAAGCTGCCGAGGCTTTCCTAGGC  
TTTTCTATGCGCCTCCCACGGACTCTTTCCTCTGA

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CGGGTCGACCCACGCGTCCGCCGGTTTCACTGCTCCCCTCAGTCTCTTTTGGGCTCTTTC  
CGGGCATCGGGACGATGACCGTCAAAGCCGAGGCTGCTCGAAGCACCCCTTACCTACTCCA

[illegible]

CCACCTGCAGCGGGAGCGCCGGTTCTCTGGAGCCCCGGGCCAGGTTCTACGCTGCTGAGGT  
GGCCAGCGCCATTGGCTACCTGCACTCCCTCAACATCATTTACAGGGATCTGAAACCAGA  
GAACATTCTCTTGGACTGCCAGGGACACGTGGTGCTGACGGATTTTGGCCTCTGCAAGGA  
AGGTGTAGAGCCTGAAGACACCACATCCACATTCTGTGGTACCCCTGAGTACTTGGCACC  
TGAAGTGCTTCGGAAAGAGCCTTATGATCGAGCAGTGGACTGGTGGTGCTTGGGGGCAGT  
CCTCTACGAGATGCTCCATGGCCTGCCGCCCTTCTACAGCCAAGATGTATCCCAGATGTA  
TGAGAACATTCTGCACCAGCCGCTACAGATCCCCGGAGGCCGGACAGTGGCCGCCTGTGA  
CCTCCTGCAAAGCCTTCTCCACAAGGACCAGAGGCAGCGGCTGGGCTCCAAAGCAGACTT  
TCTTGAGATTAAAGAACCATGTATTCTTCAGCCCCATAAACTGGGATGACCTGTACCACAA



## FIGURE 20

GAGGCTAACTCCACCCTTCAACCCCAAATGTGACAGGACCTGCTGACTTGAAGCATT TTTGA  
CCCAGAGTTTCACCCAGGAAGCTGTGTCCAAGTCCATTGGCTGTACCCCTGACACTGTGGC  
CAGCAGCTCTGGGGCCTCAAGTGCATTCTCTGGGATTTTCTTATGCGCCAGAGGATGATGA  
CATCTTGGATTGCTAGAAGAGAAGGACCTGTGAACTACTGAGGCCAGCTGGTATTAGTA  
AGGAATTACCTTCAGCTGCTAGGAAGAGCGACTCAAAC TAACAATGGCTTCAACGAGAAG  
CAGGTTTATTTTTTCCAGCACATAAAAGAAAAATAATGTTTCGGAGTCCAGGACTGGCAG  
GACAGGTCATCAGATACTCAGAGGCTGTATCTCTGCCCTGCCAACCTTGACAAATGGCTT  
CCAATGTTAGGTTTGCTACAAGATGGTTACTGGAGCTCTAGCTGCCTATTTTGTGTTTAG  
GGAAGGGAAAATGGAGGAAAGGGGAGAAGAGCAAAGGGCGCTTTTAAAGAGCTTTCCCAA  
AAGCTCCACCCAATGACTTCTGCTTCCATCTACTAACCACCCACCCCTACCTGGAATGG  
AGGCTGGGAGATGTGGCTTATTTGCTGGGTACGTGACTATCCCTAATAACAAAGGGGTTC  
TGACACTAAGACATTAGGGGAGAATGTTGGGTAGGCAGCCAGCACTCTTTTACCAGAGGG  
CCTCCTGGTGTTTGGATTTTGATCTCAATGTGTAAAATGACAGAGATGTAACAAGCTCAT  
AGGGTATCAATATCTCTTATTGTTCT

SEQ ID NO: 21\_AA887783\_H

CGGATGCATTTNTTGGTGTGCTCTTGAGGGATTAAATGCAAAGAGATCACACCATGGACT  
ACAAGGAAAGCTGCCCAAGTGTAAGNATTTCCAGCTCCGATGAACACAGAGAGAAAAAGA  
AGAGGTTTACTGTTTATAAAGTTCTGGTTCAGTGGGAAGAAGTGAATGGTTTGTCTTCA  
GGAGATATGCAGAGTTTGATAAACTTTATAACACTTTAAAAAAACAGTTTCTCTGCTANGG  
CCCTGAAGATTCCTGCCAAGAGAATATTTGGTGATAATTTTGATCCAGATTTTATTAAAC  
AAAGACGAGCAGGACTAAACGAATTCATT CAGAACCTAGTTAGGTATCCAGAACTTTATA  
ACCATCCAGATGTCAGAGCATTCTTCAAATGGACAGTCCAAAACACCAGTCAGATCCAT  
CTGAAGATGAGGATGAAAGAAGTTCTCAGAAGCTACACTCTACCTCACAGAACATCAACC  
TGGGACCGTCTGGAAATCCTCATGCCAAACCAACTGACTTTGATTTCTTAAAAGTTATTG  
GAAAAGGCAGCTTTGGCAAGGTCTTCTTGCAAAACGGAAACTGGATGGAAAATTTTATG  
CTGTCAAAGTGTTACAGAAAAAAATAGTTCTCAACAGAAAAGAGCAAAAACATATTATGG  
CTGAACGTAATGTGCTCTTGAAAAATGTGAAACATCCGTTTTTGGTTGGATTGCATTATT  
CCTTCCAAACAACCTGAAAAGCTTTATTTTGTCTGGATTTTGTTAATGGAGGGGAGGGAC  
ATGTTGTCTTAACAGATTTTGGGCTTTGTAAAGAAGGAATTGCTATTTCTGACACCACTA  
CCACATTTTGTGGGACACCAGAGTATCTTGACCTGAAGTAATTAGAAAACAGCCCTATG  
ACAATACTGTAGATTGGTGGTGCCTTGGGGCTGTTCTGTATGAAATGCTGTATGGATTGC  
CTCCTTTTTTATTGCCGAGATGTTGCTGAAATGTATGACAATATCCTTCACAAACCCCTAA  
GTTTGAGGCCAGGAGTGAGTCTTACAGCCTGGTCCATTCTGGAAGAACTCCTAGAAAAAG  
ACAGGCAAAATCGACTTGGTGCCAAGGAAGACTTTCTTGAAATTCAGAATCATCCTTTTT  
TTGAATCACTCAGCTGGGCTGACCTTGTACAAAAGAAGATTCCACCACCATTTAATCCTA  
ATGTGGCTGGACCAGATGATATCAGAACTTTGACACAGCATTTACAGAAGAAACAGTTC  
CATATTCTGTGTGTGTATCTTCTGACTATTCTATAGTGAATGCCAGTGTATTGGAGGCAG  
ATGATGCATTCGTTGGTTTCTCTTATGCACCTCCTTCAGAAGACTTATTTTTGTGAGCAG  
TTTGCCATT CAGAAACCATTGAGCAAAATAAGTCTATAGATGGGACTGAAACTTCTATTT  
GTGTGAATATATTCAAATATGTATACTAGTGCCTCATTTTTTATATGTAATGATGAAAAC  
TATGAAAAAATGTATTTTCTTCTATGTGCAAGAAAAATAGGGCATTTCAAAGAGCTGTTT  
TGATTAAAATTTATATTCTTGTTTAATAAGCTTATTTTTTAAACAATTTAAAAGCTATTAT  
TCTTAGCATTAACCTATTTTTTAAAGAAACCTTTTTTGCTATTGACTGTTTTTTCCCTCTA  
AGTTTACACTAACATCTACCCAAGATAGACTGTTTTTTAACAGTCAATTT CAGTTCAGCT  
AACATATATTAATACCTTTGTAACCTTTTGCTATGGCTTTTGTTATCACACCAAAACTAT  
GCAATTGGTACATGGTTGTTTAAGAAGAAACCGTATTTTTTCCATGATAAATCACTGTTTG  
AAATATTTGGTTCATGGTATGATCGAAATGTAAAAGCATAATTAACACATTGGCTGCTAG  
TTAACAATTGGAATAACTTTATTCTGCAGATCATTTAAGAAGTAACAGGCCGGGGCGGGT  
GGCTCACGCCTGTAATCCCAGCACTTTGGGAGGCTGAGGCGGGCAGATCACCTGAGGTCA

## FIGURE 2P

GGAGTTGGAGACCAGCCTGACCAACA/TGGACAAACCCCGTCTCTACTAAAAATACAAAAT  
TGGCAGGGTGTGGTGGCACATGCCTATAATCCCAGCTACTTGGGAGGCTAAGGCAGGAGA  
ATCGCTTGAACCCGGGAGGCGGAGGTTGCASTGAGCCGAGATCGCACCATTTGCACTCCTG  
CCTGGGCAACAAGAGTGAAACTCCATCTCC

SEQ ID NO: 22\_R47805\_H

ATGGCGCACCAAACGGGCATCCACGCCACGGAAGAGCTGAAGGAATTCTTTGCCAAGGCA  
CGGGCTGGCTCTGTGCGGCTCATCAAGGTTGTGATTGAGGACGAGCAGCTCGTGCTGGGT  
GCCTCGCAGGAGCCAGTAGGCCGCTGGGATCAGGACTATGACAGGGCCGTGCTGCCACTG  
CTGGACGCCCAGCAGCCCTGCTACCTGCTCTACCGCCTCGACTCACAGAATGCTCAGGGC  
TTCGAATGGCTCTTCCTCGCCTGGTCGCCTGATAACTCCCCCGTGCGGCTGAAGATGCTG  
TACGCGGCCACGCGGGCCACAGTGAAAAAGGAGTTTGGAGGTGGCCACATCAAGGATGAG  
CTCTTCGGGACTGTGAAGGATGACCTCTCTTTTGCTGGGTACCAGAAACACCTGTCTGCTCC  
TGTGCGGCACCTGCCCCGCTGACCTCGGCTGAGAGAGAGCTCCAGCAGATCCGCATTAAAC  
GAGGTGAAGACAGAGATCAGTGTGGAAAGCAAGCACCAGACCCTGCAGGGCCCTCGCCTTC  
CCCCTGCAGCCTGAGGCCCCAGCGGGCACTCCAGCAGCTCAAGCAGAAAATGGTCAACTAC  
ATCCAGATGAAGCTGGACCTAGAGCGGGAAACCATTGAGCTGGTGCACACAGAGCCCACG  
GATGTGGCCCAGCTGCCCTCCCGGGTGCCCCGAGATGCTGCCCGCTACCACTTCTTCCTC  
TACAAGCACACCCATGAGGGCGACCCCCCTTGAGTCTGTAGTGTTCATCTACTCCATGCCG  
GGGTACAAGTGCAGCATCAAGGAGCGAATGCTCTACTCCAGCTGCAAGAGCCGCCTCCTC  
GACTCCGTGGAGCAGGACTTCCATCTGGAGATCGCCAAGAAAATTGAGATTGGCGATGGG  
GCAGAGCTGACGGCAGAGTTCCTCTACGACGAGGTGCACCCCAAGCAACACGCCTTCAAG  
CAGGCCTTCGCCAAGCCCAAGGGGCCAGGGGGCAAGCGGGGCCATAAGCGCCTCATCCGC  
GGCCCGGGTGAAAATGGGGATGACAGCTAG

SEQ ID NO: 23\_H60215\_H

CCACGCGTCCGGCGCCGCAGCCATGGAGGGAGGCGGCGGCGGCGGCGGCGGCGGCTCGGG  
TGGCTGCGCTGGGAGGCGGCGGTGAGAGGCTCGCACGCCTCCAGCCCCGGCCCCCGCCCC  
CGGGAGGGAGAGCCGAGCAGCCCCGGCTCTGGGCTACGGACTATGGGCGAATAGCTCTGA  
CCACCCGGCGAAGTGCACACACCCAGAAGCTATGTCCTTCGGCAGTAAAAGTTTACAGC  
ACAATATATGTGCTCTGCTCTCCTCCCGCAATCCTGCTCCAAGAGATCTTAAGCTGGAGG  
CACCAGGTCTGAATTCCAGACTCCTCCCCACCACCCACACTTCACCTCCAACCTGGAGCAT  
GACCACAGACCCATTCCAGGGAGGCTGGCGGACTCTTCATCCTGGACAGTCCCTTACTGTA  
TGTCAAAGCTGAGAATGAAGCGGAGAGCATCAGACAGAGGAGCTGGGGAAACGTCCGCCA  
GGGCCAAGGCTCTAGGAAGTGGGATTTCTGGAAATAATGCAAAGAGAGCTGGACCATTCA  
TCCTTGGTCCCCGTCTGGGCAACTCACCGGTGCCAAGCATAGTGCAGTGTTTGGCGAGGA  
AAGATGGCACGGATGACTTCTATCAGCTGAAGATCCTGACCCTGGAGGAGAGGGGGGACC  
AAGGCATAGAGAGCCAGGAAGAGCGGCAGGGCAAGATGCTGCTGCACACCGAGTACTCAC  
TGCTGTCTCTCCTGCACACGCAGGATGGCGTGGTGCACCACCACGGCCTCTTCCAGGACC  
GCACCTGTGAAATCGTTGAGGACACAGAATCCAGCCGGATGGTTAAGAAGATGAAGAAGC  
GCATCTGCCTCGTCCTGGACTGCCTCTGTGCTCATGACTTCAGCGATAAGACCGCTGACC  
TCATCAACCTGCAGCACTACGTCAATCAAGGAGAAGAGGCTCAGCGAGAGGGGAGACTGTGG  
TAATCTTCTACGACGTGGTCCGCGTGGTGGAGGCCCTGCACCAGAAAAATATCGTGACCA  
GAGACCTGAAGCTGGGGAAACATGGTGCTCAACAAGAGGACACATCGGATAACCATCACCA  
ACTTCTGCCTCGGGGAAGCATCTGGTGAGCGAGGGGGACCTGCTGAAGGACCAGAGAGGGA  
GCCCTGCCTACATCAGTCCCGACGTGCTCAGCGGCCCGGCCGTACCGTGGCAAGCCCAGTG  
ACATGTGGGCCCTGGGCGTGGTGCTCTTACCATTGCTGTATGGCCAGTTCCCCTTCTACG  
ACAGCATCCCGCAGGAGCTCTTCCGCAAGATCAAGGCTGCCGAGTATACCATTCCTGAGG  
ATGGACGGGTTTCTGAGAACACCGTGTGTCTCATCCGGAAGCTGCTGGTCCCTTGACCCCC  
AGCAGCGCCTGGCCGCGCCGACGTCCTGGAGGCCCTCAGTGCCATCATTGCATCATGGC



## FIGURE 2Q

AGTCCCTGTCATCTCTGAGTGGGCCTTTGCAAGTGGTTCCTGACATTGATGACCAAATGA  
GCAATGCGGATAGCTCCCAGGAGGCGAAGGTGACGGAGGAGTGCTCCCAGTACGAGTTTG  
AGAACTACATGCGTCAGCAGCTGCTGCTGGCCGAGGAGAAGAGCTCCATCCATGACACCC  
GGAGCTGGGTACCCAAGCGGCAGTTCGGCAGCGCACCCACCGGTGCGACGGCTGGGCCACG  
ACGCACAGCCCATGACCTCCTTGGACACGGCCATCCTGGCGCAGCGCTACCTGCGGAAAT  
AACAGCCTCAGCCGGGGGCCACCAGCACTGCTGCCACTTCTTCCAGCCCCAGCCAAAGGCC  
TGGCTGTCAGGGCTGGGCCCTGTAGTGCTGGACTCTCCCGGGCCACAATAGGGACAGGGC  
AGGGACAGGGACAGCCCAGGTCACACGTGGGGTCAGCAGAGGTACCACGAAGCTACCTTT  
TGGGATGATTGCTCGATTGTTTGGTTTTTAAATCTGAGAAGCCTAGATAACTAATCTGCT  
TTTAATCACGATGTTTTAATCTACCTCTGTCTCTTTAACCATGCTGTCTCTGGACTGAGC  
AAGAGGGAGGAGGGAGCCTGCTCACCCCACTCCAGGGCCTTCCCCAGCGGCCACCAACTG  
ACCTGGGGCGCTGCTCCCCACAGTCCAAATAAGCTGAAAGTGACGCTCGCTGCAGGCCCC  
AGAGCGAGCTTCCCCTCCTCCCTGCTCTCCAGGCCCCCTGCCACAGCCTCTTTCCGTCCC  
TCTCTTTCTGATCCAGGCCCCCTCAGTCCAAGCTTTGGAAAACCTTCACCTCATCTTAAAC  
CAAACCTCAAATATATTTATTTTTTTTACCAT

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GCCGCGATGGCCAGCACCCAGGAGTATCGAGCTGGAGCACTTTGAGGAACGGGACAAAAGG  
CCGCGGGCCGGGGTCCGCGGAGAGGGGGCCCCCAGCTCCTCCGGGGGGCAGCAGCAGCTCGGGC  
CCCAAGGGGAACGGGCTCATCCCCAGTCCGGCGCACAGTGCCCACTGCAGCTTCTACCGC  
ACGCGGACCCTGCAGGCCCTCAGCTCGGAGAAGAAGGCCAAGAAGGCGCGCTTCTACCGG  
AACGGGGACCGCTACTTCAAGGGCCTGGTGTGTTGCCATCTCCAGCGACCGCTTCCGGTCC  
TTCGATGCGCTCCTCATAGAGCTCACCCGCTCCCTGTCCGACAACGTGAACCTGCCCCAG  
GGTGTCCGCACTATCTACACCATCGACGGCAGCCGGAAGGTACCAGCCTGGACGAGCTG  
CTGGAAGGTGAGAGTTACGTGTGTGCATCCAATGAACCATTTTCGTAAAGTCGATTACACC  
AAAAATATTAATCCAAACTGGTCTGTGAACATCAAGGGTGGGACATCCCGAGCGCTGGCT  
GCTGCCTCCTCTGTGAAAAGTGAAGTAAAAGAAAGTAAAGATTTTCATCAAACCCAAGTTA  
GTGACTGTGATTGGAAGTGGAGTGAAGCCTAGAAAAGCCGTGCGGATCCTTCTGAATAAA  
AAGACTGCTCATTCCCTTTGAACAAGTCTTAACAGATATCACCGAAGCCATTAAACNAGCC  
TCAGGAGTCGTCAAGAGGCTCTGCACCCTGGATGGAAAGCAGGTGAGAGTTACGTGTGTG  
CATCTGCCAGACTTTTTTTGGTGATGACGATGTTTTTTATTGCATGTGGACCAGAAAAATTT  
CGTTATGCCCAAGATGACTTTGTCCCTGGATCATAGTGAATGTCGTGTCCTGAAGTCATCT  
TATTCTCGATCCTCAGCTGTTAAGTATTCTGGATCCAAAAGCCCTGGGGCCCTCTCGACGC  
AGCCAGATTTCTGCTCATGGCAGATCTTCTTCCAATGTAAACGGTGGACCTGAGCTTGAC  
CGTTGCATAAGTCCTGAAGGTGTGAATGGAAACAGATGCTCTGAATCATCAACTCTTCTT  
GAGAAATACAAAATTGGAAAGGTCATTGGTGTGATGGCAATTTTGCAGTAGTCAAAGAGTGT  
ATAGACAGGTCCACTGGAAAGGAGTTTGCCCTAAAGATTATAGACAAAGCCAAATGTTGT  
GGAAAGGAACACCTGATTGAGAATGAAGTGTCAATACTGCGCCGAGTGAAACATCCCAAT  
ATCATTATGCTGGTTCGAGGAGATGGAAACAGCAACTGAGCTCTTTCTGGTGTGGAATTG  
GTCAAAGGTGGAGATCTCTTTGATGCAATTACTTCGTGACCAAGTACACTGAGAGAGAT  
GGCAGTGCCATGGTGTACAACCTTAGCCAATGCCCTCAGGTATCTCCATGGCCTCAGCATC  
GTGCACAGAGACATCAAACCAGAGAATCTCTTGGTGTGTGAATATCCTGATGGAACCAAG  
TCTTTGAAACTGGGAGACTTTGGGCTTGCGACTGTGGTAGAAGGCCCTTTATACACAGTC  
TGTGGCACACCCACTTATGTGGCTCCARAAATCATTGCTGAAACTGGCTATGGCCTGAAG  
GTGGACATTTGGGCAGCTGGTGTGATCACATACATACTTCTCTGTGGATTCCCACCATTC  
CGAAGTGAGAACAATCTCCAGGAAGATCTCTTCGACCAGATCTTGGCTGGGAAGCTGGAG  
TTTCCGGCCCCCTACTGGGATAACATCACGGACTCTGCCAAGGAATTAATCAGTCAAATG  
CTTCAGGTAAATGTTGAAGCTCGGTGTACCGCGGGACAAATCCTGAGTCACCCCTGGGTG  
TCAGATGATGCCTCCCAGGAGAATAACATGCAAGCTGAGGTGACAGGTAAACTAAAACAG  
CACTTTAATAATGCGCTCCCCAAACAGAACAGCACTACCACCGGGGTCTCCGTTCATCATG

## FIGURE 2R

GTGAGTGGGAAGGGCGGAGGTCTGGCCTGACTGCGGAGCCGGCCTTGAAGTTTTTGAATTA  
GGTAGCCGGGAGCTGCCCTCACATGGAAGTTGGTGCCTTCCGTAGTCCTATTTTCATATGA  
AGATTGGCTTGGCATGTGGAGGGCACTCATTCGGCAACTCCCAGGCTTTGGGGCACTGTGT  
GGAGGGGCTTGTGTAGGGACCAGCAGGCCTGGTGTGAGGGGTCCAGGCGTCAAGGAGCTC  
CTGGCTGGGCCCTCTGGGCAGCTGCTTCCACTCTTGTCTCTGCCTTCTCATCTAGAGAGA  
CTCCCAAGCCCTGGAGGGGTGTGTTGTGTTAGGAATTAAGTCCCTGCCTACCCCAAGGCC  
TCAGAAATAGATTATTAGAGATGTGAATTATTCTTTGAGACTTGGGATAAGAAACAGCCA  
AAGCTAAACATATTTTCAAGTTTTAAAAAATCAGTGTTTTTATAAAACACAGTTTGGGGCTTT  
TAAAGGTACATAATCAAGGAAAAAAATATATATTCATTTTTCAGGGTTGGTAACATTTTA  
TGAGATGTCAGTGACAACGATGGCCTTATTTTTTTTCAGCCTTTTCTTCTTCCAAAATGTT  
TCTTAAGGCAACTCTCCTAAATACATAAACACAACAAATTAATAATGAAAAGTGACATGAG  
AGTAAATGAATCAAAAGGAAAAAACATTGAACCAGAGGTGAGGGCAGCACACCCGCAGCA  
GCTGTCCAGGCCTGAGCCAATGCAACCCTGGGCGGGAAGGCCAGCTCACCGTGAGCAGGT  
AGAAGCCAGCCAGCCACCCAGGCAGGGACCTTGGTTCTCCCCACACACTCCCAGGAGCAG  
GGAACAGGGGTGGAGTGGCCTTTCCCAGAGCTGGAGTTGGCTGCAGCAGCTTTTGAATCA  
GACCTGCCAAGGTGATGGGCGTCTGAGTTTCACATCTGGGCCCCCGTGACCCCACTGAG  
TCCTGACAGCTAAGGATGGGCCACCTCCACAGCTCCGTCACCTCGTACTTGGGACAGGCCT  
CTCATCCTCTGGGAAGGTCCTCCTTGTTCCTACCCAACTAGAAGGGAAACAGTGGCATA  
TTCTCATGGTACATGGTTGTCTGAAAGCCTTACCTAGGAAGACGCAGGGTCTAGATAGAA  
GCTATAAGGAAGCCACACACATAACCCACATCCCCACACCCCCAACATCCCCCACACTCC  
CCACACCCCCCACACCCCCCACATCCCCACCATAATTACCCCCACCTCCAAATATCTCAT

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ACCAAGTCCTCCAGCTCCTCTCCAACCAGCCCGGGAAGTTTCAGAGGATTGAAGATTTCT  
GCTCAGGGCAGATCTTCTTCCAACGTAAACGGTGGGCCTGAACTTGACCGTTGCCTGAGC  
CCTGAAGGTGTGAATGGAAACCGGTGCTCCGAGTCGTTCCCCCTTCTGGAGAAATACAGA  
ATAGGGAAGGTCATCGGGGACGGCAACTTCGCGGTAGTTAAGGAGTGCGTGGACAGGTAC  
ACTGGAAAAGAGTTTGCATTAAAGATTATAGACAAAGCCAAATGCTGTGGAAAGGAGCAT  
CTGATTGAGAACGAAGTGTCAATCCTGCGCCGAGTGAAGCACCCCAACATCATCATGTTG  
GTTGAAGAGATGGAAACAGCAACTGACCTCTTTCTAGTGATGGAACCTGGTCAAAGGTGGA  
GATCTCTTTGATGCGATTACCTCTTCAACCAAGTACACTGAGAGAGATGGAAGCGCCATG  
GTGTACAACCTAGCCAATGCCCTCCGGTACCTGCACAGCCTCAGCATCGTCCACAGGGAC  
ATCAAGCCTGAGAATCTGCTGGTGTGCGAATACCCAGATGGAACCAAGTCTTTGAAGCTG  
GGAGACTTTGGGCTGGCGACGGTGGTTGAAGGCCCGTTGTACACGGTCTGTGGCACGCCA  
ACTTATGTGGCACCAGAGATCATAGCTGAAACAGGTTATGGCCTGAAGGTGGATGTTTGG  
GCAGCTGGTGTGATTACATACTACTTCTCTGTGGATTCCCACCATTCGCGAGTGAGAAC  
AATCTCCAGGAAGATCTCTTTGACCAGATCTTGGCTGGAAAGCTGGAATTCCCAGCCCCC  
TACTGGGACAACATTACAGACTCTCCTTGTGTGTGTTTTAGGAAATGCTTATGAAGCTGG  
CCCGTGGGCTTCCCAGTGGGACGTGCAGCAGTTCTTGGCAGAGCAGGGCCAGCTCTGCTG  
TGTCATCTCCAGGGTCTCCCATCACCTCTGCTCTTTGCCATGGCAGGTCTGCTGAGACCC  
CGCGGGGACGGGGGCATGGTGTCTCCCTGATTGGCCTGTGACCAACCTTCTGGAAGGCTGC  
TGGCAGTTTTTCCCTGTTTTTCCACCACCCCACTCTTTTTTAATAATTGTATATAACTGTACT  
TGTTCTACTTGCTTGTCTTTAAACAGGGGGCCCCCACAGTTCCTCTCACTGTTAGATTT  
TGCCTTTTCCAGGTATCCCCAACCTGCAATAAACTCTTCCCTCTTCAG

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CCAGCAGCCAAGAGGGTAGTGGTGTACCGGAATGGGGACCCATTCTTCCCAGGCTCCCAG  
CTGGTGGTGAATCAACGCCGCTTCCCCACCATGGAGGCCTTCTCTGCGAGGTGACATCA  
GCTGTGCAGGCCCCCACTGGCTGTGCGTGCCCTCTACACACCTTGTCATGGCCACCCTGTC  
ACCAACCTGGCAGACTTGAAGAACAGAGGGCAGTATGTGGCCGCTGGATTTGAACGATTTC

## FIGURE 2S

CACAAGCTCCCCCCTTACCAGGCTTTTTGTCTCAGTGTGTTTCAGGAATGGGGACCTGGTA  
AGTCCCCCATTTAGTCTGAAGCTGTCCCAGGCTGCCAGCCAGGACTGGGAAACTGTCTT  
AAGCTCCTGACTGAGAAGGTCAAGTTGCAGAGTGGGGCTGTGAGACTCTGCACCCTAGAG  
GGGCTCCCACCTGTCAGCAGGGAAGGAGCTGGTAACTGGCCATTACTATGTGGCTGTGGGA  
GAGGATGAGTTCAAGGACCTTCCCTATCCAGCTCTGTCCACAAGAGGGCTCCTGGCAGCA  
GGCAATGAAGCCCACCTGAGGAGTGGAGTGGGGACTGTGCTGCTGGTTCCCCCAAGCCTCTT  
GGAAGGAAGGCTAAGAAGGAGACATGCCTAATCGTGACCCCTGACCCCTGAAATACCAGCAG  
TCAGAAACAAGCAGAGACGGGCAATCATTTCCCATCAGGAGTTATAGGAGTATATGGAGCT  
CCCCACCGAAGGAAGGAGACAGCGGGGGCCCTGGAAGTAGCAGATGATGAAGACACTCAG  
ACAGAGGAGCCCTTGGATCAGAGGGCAGCACAGATAGTGGAACAGGTTACTTGTCTGCAA  
GACTTTTTTGGTGATGACGATGTTTTTATTGCATGTGGACCAGAAAAATTTTCGTTATGCC  
CAAGATGACTTTGTCTGCTGGATCATAGTCGTGACGGCTCCTGAGAGAGCACCAGGCGGGC  
TTTGAGAAGCTCCGCAGGACCCGAGGAGAAGAGAAGGAGGCAGAGAAGGAGAAAAAGCCA  
TGTATGTCTGGAGGCAGAAGGATGACTCTCAGAGATGACCAACCTGCAAAGCTAGAAAAG  
GAGCCCAAGACGAGGCCAGAAGAGAACAAGCCAGAGCGGCCAGCGGTGCGAAGCCACGG  
CCCATGGGCATCATTGCCGCCAATGTGGAAGGCATTATGAGACTGGCCGGGTGCTATTGGG  
GATGGGAACCTTTGCTGTCTGTAAGGAGTGCAGACACCGCGAGACCAGGCAGGCCTATGCG  
ATGAAGATCATTGACAAGTCCAGACTCAAGGGCAAGGAGGACATGGTGGACAGTGAGATC  
TTGATCATCCAGAGCCTCTCTCACCCCAACATCGTGAAATTGCATGAAGTCTACGAAACA  
GACATGGAAATCTACCTGATCCTGGAGTACGTGCAGGGAGGAGACCTTTTTTGACGCCATC  
ATAGAAAGTGTGAAGTTCCCGGAGCCCGATGCTGCCCTCATGATCATGGACTTATGCAAA  
GCCCTCGTCCACATGCACGACAAGAGCATTGTCCACCGGGACCTCAAGCCGGAAAACCTT  
TTGGTTCAGCGAAATGAGGACAAATCTACTACCTTGAAATTGGCTGATTTTGGACTTGCA  
AAGCATGTGGTGAGACCTATATTTACTGTGTGTGGGACCCCAACTTACGTAGCTCCCGAA  
ATTCTTTCTGAGAAAGGTTATGGACTGGAGGTGGACATGTGGGCTGCTGGCGTGATCCTC  
TATATCCTGCTGTGTGGCTTTCCCCCATTTCCGCAGCCCTGAXXGAGGGGACCAGGACGAG  
CTCTTTAACATCATCCAGCTGGGCCACTTTGAGTTCCTCCCCCCTTACTGGGACAATATC  
TCTGATGCTGCTAAAGATCTGGTGAGCCGGTTGCTGGTGGTAGACCCCAAAAAGCGCTAC  
ACAGCTCATCAGGTTCTTCAGCACCCCTGGATCGAAACAGCTGGCAAGACCAATACAGTG  
AAACGACAGAAGCAGGTGTCCCCCAGCAGCGATGGTCACTTCCGGAGCCAGCACAAGAGG  
GTTGTGGAGCAGGTATCATAGTCACCACCTTGGGAATCTGTCCAGCCCCCAGTTCTGCTC  
AAGGACAGAGAAAAGGATAGAAGTTTGAGAGAAAAACAATGAAAGAGGCTTCTTCACATA  
ATTGGTGAATCAGAGGGGAGAGACACTGAGTATATTTTAAAGCATATTAAAAAAATTAAGT  
CAATGTTAAATGTCACAACATATTTTTTAGATTTGTATATTTAAAGCCTTTAATACATTTT  
TGGGGGGTAAGCATTGTCTCAGTGAGGAATTTTGGTAATAATGATGTGTTTTGCTTCCC  
CTTTGTAACCAAGTTTATTCTGTACTACAGGAGTGGTGCTTACCAGGGTCTAAACTCCCC  
CTGTGAGATTAATAAGGTGCATTG

SEQ ID NO: 28\_AA197883\_M

ATGCCAACCGCGCCGGTCTGCGCCCCGCCGCCGCCAGCGACCCCCGCCCGCCGGCA  
CCCAGTCGCCCTGCGCCTCCCATTTCCGGGGCCACCGAGGCCCATGTGACCATTCTCTGAAA  
TGCTTAAGCTCGAAGATCTCTGAGAGAAAGCTGCCAGGCCCCCTGGTTACCTGCGGGACGA  
GGACCTCTGGAGAAGCCAGTTCTGGGGGCCACGTGGTGCCGTCATGCCGCTGTTTCAGCCCT  
CAGAGCAGCCTCCACTCAGTCCGCGCAGAGCACAGCCCCTGAAGCCCAGGGTGGTGACG  
GTGGTGAAGCTGGGTGGGTCAGCCCCCTCCGTAAGGCCACCCTGCTCCTCAACCGGCGCTCA  
GTGCAGACCTTTGAGCAGCTCCTATCAGACATCTCCGAAGCCTTGGGCTTCCCACGCTGG  
AAGAACGACCGTGTGCGGAAGCTGTTCAACCTCAAGGGCAGGGAGGTGAAGAGTGTGTCT  
GACTTCTTCCGGGAGGGTGATGCTTTTCATAGCTATGGGCAAAGAGCCGCTGACATTGAAG  
AGTATCCAGTTGGCCATGGAGGAGCTGTATCCTAAGAACCAGGGCTCTTGCCCTGGCCCCCT  
CACAGTAGAGTCCCCTCCCCAAGGCTGAGAAGCAGACTTCCCAGCAAGCTTCTGAAAGGA



## FIGURE 21

AGTCACCGCTGTGGGGAGGCGAGGAAGCTATAGCGCGGAAATGGAGAGTAAGGCAGTCTCT  
AGGCATCAGGGCAAGACTTCCACAGTGCTGGCCCCAGAAGACAAGGCGAGGGCCCCAGAAG  
TGGGTAAGAGGGGAAACAGGAGTCAGAACCTGGTGGCCCCGCCTTCACCCGGGGCAGCCACT  
CAGGAGGAGACTCATGCAAGTGGAGAGAAACATCTGGGGGTGGAGATCGAAAAGACCTCC  
GGGGAGATTGTCAGATSTGAGAAGTGTAAGAGAGAAAGAGAGCTGCAGTTGGGCCTGCAG  
AGGGAGCCGTGCCCCGCTGGGAACCAAGTGAGCTGGACCTGGGGAGAGCTCAGAAGAGGGAT  
TCCGAGAAGTTGGTGAGGACCAAGAGCTGCAGGAGGCCTTCTAAGGCAAAATTTACAGAT  
GGAGAGGAAGGGTGGAAGGGTGACAGCCATCGGGGCAGTCCCAGGGACCCCCCTCAGGAA  
ATGAGGAGGCCCCAACAGCAACTCAGACAAGAAAGAGATCAGAGGCTCAGAAAGTCAGGAC  
AGTTATCCTCAGGGGGCACCCAAGGCCCCAGAAGGACTTCGTGGAAGGGGCCACCAGCTGTA  
GAGGAGGGGGCCGATAGACATGAGGAGAGAGGACCGGCACACATGCAGGAGCAAGCATGCC  
GCCTGGCTCCGGAGAGAGCAGCAGGCCGAACCCCCACAGCTCCCCAGAACCCGAGGGGGAG  
GAGAAGCAAGCAGAGCACGAGAAGAAGCCAGGCGGCTTAGGAGAGAGGAGGGGCGCCAGAG  
AAGGAGTCTAAGAGGAAGCTAGAAGAGAAGAGGGCCAGAACGACCCAGTGGCCGGAAGCCG  
AGGCCCAAGGGCATCATCTCAGCGGATGTGGAGAAGCACTATGACATAGGTGGGGTTCATT  
GGGGATGGCAACTTTGCCACCGTGAAGGAATGCAGGCACCGAGAGACCAAGCAGGCTTAC  
GCCATGAAGATGATTGACAAGTCCCAGCTGAAGGGTAAGGAGGACATTGTGCGACAGTGAG  
ATTTTAATCATCCAGAGTCTCTCTCATCCCAACATTGTGAAACTGCATGAGGTCTACGAA  
ACGGAGGGCGGAGATCTACCTGATCATGGAGTATGTGCAGGGAGGGGACCTTTTTTGATGCC  
ATCGTTGAAAATGTGAAGTTTCCAGAGCCCGAGGCTGCAGTTATGATCACAGACTTGTGT  
AAGGCCTTCGTCCACATGCACGACAAGAATATCGTCCACCGGGACGTGAAACCAGAAAAC  
CTCCTGGTTTCAGCGAAATGAAGACAAGTCTATCACCTTGAAGCTGGCTGATTTTGGCTTG  
GCCAAATATGTGGTGAGGCCTATATTTACTGTGTGTGGGACGCCAACATATGTAGCTCCT  
GAAATTCTTTCTGAGAAAGGTTACGGCCTGGAGGTGGACATGTGGGCGGCAGGTGTGATC  
CTATACATCCTCTTGTGTGGCTTCCCCCCTTTCCGAAGTCTTGAGAGGGACCAAGACGAG  
CTCTTCAACATCATCCAAGTGGGCCAGTTTGAGTTCCTCTCTCCTTACTGGGACAACATT  
TCTGATGCTGCCAAAGATCTGGTGAGAAATTTGCTGGAGGTGGACCCTAAGAAGCGGTAC  
ACGGCCGAACAGGTCCTACAGCATCCCTGGATTGAGATGGTTGGGCATACCAACACAGGG  
AACTCACAGAAGGAGGAGTCCCCCAACAGTTTAGGTCACTTCCAGAGTCAGCACAAGAAG  
GTTGCAGAGCAGATGCCATAA

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CTCCGCTGCTGTGCGCCAGGAGTCACTTCACGAGAAGCCAGGTCACAACCGTCGGGCCCTTG  
TCTGGAAAAGTAAAAGTGGATCCTGCCACGTTTCGGAGCTCCCTGGCGCCTCGCCCCGGCTG  
GAGCTAGAGAACTCGTCCTGTGGCGGGCCCCCGGCGTGGGGCGGGACAGCGGCCCCCTGGA  
GGGGGCAGTCCCGGGAGAACCTGCGGGCGGCCGGAGCGGTAAAAATAAGTGAATAAGAAG  
CAGACCTGGGAATCACCTAACATGTCGAGGAGGAGATTTGATTGCCGAAGTATTTTCAGGC  
CTACTAACTACAACCTCCTCAAATTTCCAATAAAAAATGGAAAACCTTTAATAATTTCTATATA  
CTTACATCTAAAGAGCTAGGGAGAGGAAAATTTGCTGTGGTTAGACAATGTATATCAAAA  
TCTACTGGCCAAGAATATGCTGCAAAATTTCTAAAAAAGAGAAGAAGAGGACAGGATTGT  
CGGGCAGAAATTTTACACGAGATTGCTGTGCTTGAATTGGCAAAGTCTTGTCCCCGTGTT  
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GCAGGTGGAGAAATTTTCAGCCTGTGTTTACCTGAGTTGGCTGAAATGGTTTCTGAAAAT  
GATGTTATCAGACTCATTAACAAATACTTGAAGGAGTTTATTATCTACATCAGAATAAC  
ATTGTACACCTTGATTTAAAGCCACAGAATATATTACTGAGCAGCATATACCCTCTCGGG  
GACATTAAAATAGTAGATTTTGGAAATGTCTCGAAAAATAGGGCATGCGTGTGAACTTCGG  
GAAATCATGGGAACACCAGAATATTTAGCTCCAGAAATCCTGAACTATGATCCCATTACC  
ACAGCAACAGATATGTGGAATATTGGTATAATAGCATATATGTTGTAACTCACACATCA  
CCATTTGTGGGAGAAGATAATCAAGAAACATACCTCAATATTTCTCAAGTTAATGTAGAT  
TATTCGGAAGAACTTTTTTCATCAGTTTCACAGCTGSCCAGAGACTTTATTTCAGAGCCTT

## FIGURE 2U

TTAGTAAAAAATCCAGAGAAAAGACCAACAGCAGAGATATGCCTTTCTCATTTCTTGGCTA  
CAGCAGTGGGACTTTTGAAAACCTTGTTTCACCCTGAAGAACTTCCAGTTCCCTCTCAAACCT  
CAGGATCATTTCTGTAAAGGTCCTCTGAAGACAAGACTTCTAAATCCTCCTGTAATGGAACC  
TGTGGTGATAGAGAAGACAAAGAGAATATCCCAGAGGATAGCAGCATGGTTTCCAAAAGA  
TTTCGTTTCGATGACTCATTACCCAATCCCCATGAACTTGTTTCAGATTTGCTCTGTTAG  
CACTTTTTTCTTTGACTCATTGGAAGTGAATTTGAAATTTTATATCCACTCCAGTGAGAT  
TATGATTTGTAGCTTCATATATGACATGTTTATATTGTAAATGCACTTTTCCATGGAATA  
ATTTAGGGAAGTGTTTAAATGTAAATTACTAGTTGCTAGCATGTTATGATTTTCATATCC  
TGAGATAGCTCTGCAGATAAGAAAATATTTAAATATATGACAAAAAGTAAAATTGTACAT  
GTGAAAG

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CCAGACGCGGCTGCACTTTTCAAACCTCAACTGTAAGAAGCGTCGGTCAGCGTCTGTGCG  
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GAGTGCGAGGTAAAAGTCTGCCTAGAGAAGCAGGTCTGGCAGTCATCAACATGTCTCGGA  
GGAGATTCGATTGCCGAAGTGTCTCAGGCTTGCTAACTACAACCCCTCAAACGCCGATTA  
AAACAGAGAATTTTAATAATTTCTATACTCTTACCCCAAAGAACTTGGGAGAGGAAAAT  
TTGCTGTGGTTAGACAATGTATATCAAATCAACTGGACAAGAGTATGCTGCCAAATCCC  
TGAAAAAGAGGAGAAGAGGGCAGGATTGCCGGGCGGAAATTCTGCATGAGATAGCTGTGC  
TGGAGCTGGCCAGGTCTTGTCCTCCACGTGATTAATCTGCATGAGGTCTACGAAAATGCAA  
CGGAAATCATTTTGGTGTTAGAATATGCTGCGGGTGGAGAAATTTTCAACCTGTGTTTAC  
CTGAGTTAGCCGAAATGGTATCTGAAAATGATGTTATCAGACTCATTAAACAAATCCTTG  
AAGGAGTTCATTATCTACATCAGAATAACATTGTTCACCTTGATTTAAAGCCACAGAATA  
TACTTTTGAGCAGTATATACCACTCGGGGACATAAAAATTGTAGATTTTGGAAATGTCTC  
GAAAAATTGGGAATGCAAGTGAGCTTCGGGAAATCATGGGAACACCTGAATACTTAGCTC  
CAGAAATCCTCAACTATGATCCCATTACCACAGCAACAGATATGTGGAATATTGGCATAA  
TAGCGTATATGTTGTTAACTCATACTACCATTTGTAGGAGAAGATAATCAAGAAACAT  
ATCTGAATATTTCTCAAGTGAATGTAGATTATTCAGAAGAAATGTTTTTCATCAGTTTCAC  
AGCTGGCCACAGACTTCATCCAGAGCCTTCTAGTAAAGAACCAGAGAAAAGACCAACAG  
CAGAAATCCTGCCTATCCCACTCATGGCTGCAGCAGTGGGACTTTGGAAGCTTGTTTCATC  
CTGAGGAAACTTCAGGCTCCTCTCAAATTCAGGATCTGACTCTCAGGTCTCTGAAGAGA  
AGACCTCCAAGTCCTCCTGTAATGGGAGCTGTGGAGCCCGGGAGGACAAGGAGAACATCC  
CTGAAGATGGCAGCTTAGTTCCTAAAGATTTTCGATTTCGATGACTCCTTGCCCAGCCCCC  
ATGAACTTGTTCCAGATTTGTTCTGTTAGCATTTTTTCTCTGTGACTCATCTGGACTGACT  
CGGAAATTTGAAATCTCTGGTGTGAGATTGTGTTTGTAGCTTCATATATTATGTTTATAT  
TATAAATGCACTTCTGCTTAGAAGAACTTAAGGAACAGTTTAAATGCTAGGCTTCTGTTG  
GCTAGCATATCATTTCTTGTCCTGAAATTGTTTTGCAGAGGAAAATATTTAAGTATATGA  
CAAAAAATGTAAATTGTGTTTAAGAGAACACATGCAACTGAAAGAACTCAAGTTCAGTCA  
GACTTATAAAATGGGTTATATTATGGTTAGTAAAAGTTGAAAAAAAATGAAAACAGGAAT  
TTAGTAGGTTCTAAGGTAAGCCCTATACCATAACTCTATTACAGAGAATCTGTTTGGGGA  
AATGCTGTCAAGGGTAAACCACAACATATACTGCTTTATAAATACTCCAGAGAGAGTTTA  
TAGTTGAAAGTATTTCCAGTTACCAATAATAGCTTGAAACTGTAAGATTTTCTTTGTGT  
GCCATGTGCTCGGTGAGAGGACACAGTCAACCAGAGCAGGGTTGATCCAGGCTGTTTCTC  
TGCAAACCGAGTCAAACTCGACATCATTTCCAGCTCATGTATTTTGTACGTGCATCATA  
TATCAGATCTAATAAGATCTGGAAGATGGATATGCAAATAAGAGGCCTTTGTCTTCTAGA  
ATGATTAGAGTAGAGGAGAATTGGATAGTACAGAATATGCTCTAGTTTTCAGTCAGACATA  
TTCATAAAGGGAAATGTTAAGTTCTGGCAGCTGACTTAGTGTTGGATGTCTCCTAAGTCT  
CAGGATAGAAGCCCATCATTAGAGCATAGGCACTTCAGGAATTCTTGTGTGAAATTCTAG  
TGAGTGAGGAGGTGTGACATGCAGCTATCTTTGGGCTCCTTTTGTGTGTGTTCTGCTGGA  
CACAACACATGGGAGTGTTCAAGTGTTCGTGGTCAATATCTATGTTTCAGTCCTGATGG

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## FIGURE 2V

GAGGGGCGCTAGGGACTGCTTTGGAGATTTCCCACTGGTGTCCATTTTAAGGTCTGTAATA  
ATGTCATGTTAAGATAACAGATCTCATAAATATGCTACTCTATCAGACTCCGTTGCCAAA  
ACAAATTAAAAGCCTGTGTATTGAAGTGGGTGTTAGTCTAACAACCTGTAAATTCTTGAA  
ATTGTTACTAAAATTCCAAATTCTTTAGATAACTTTAAACTATTTAAATTGAGCATTGCT  
GTCTTTGTTTGATTAAAGGTTGAGTTCCTTTATATCTGTATTTTTTTAAAGGAAAAGTTGT  
TTGCCTTTTGTATATGTGTGTGCATATGTGTATGTGTACAGGTATATGTATATATGTATT  
GATAGATAAAATACAGCCTTTAAACAACCTTC

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ATGATCCCTTTGGAGAAGCCAGGCAGCGGGCGGCTCCTCCCCAGGCGCCACCTCAGGCTCG  
GGCCGGGCAGGCCGGGGTCTGAGCGGGCCGTGCCGGCCGCCGCCGCCGCCAGGCCCGC  
GGGCTGCTGACAGAGATACGCGCCGTGGTGCGCACCGAGCCCTTCCAGGACGGCTACAGC  
CTGTGCCCCGGGCCGGGAGCTGGGCAGGGGGAAATTTGCAGTGGTGAGAAAATGTATAAAG  
AAAGATTCTGGGAAAGAATTTGCTGCAAAGTTCATGAGAAAAAGAAGAAAAGGCCAAGAT  
TGTCCGATGGAAATAATTCATGAGATTGCTGTACTTGAACTAGCACAAAGACAATCCTTGG  
GTCATTAATTTACATGAAGTTTATGAGACTGCATCAGAAATGATCTTAGTTCTGGAATAT  
GCTGCTGGGGGTGAAATCTTTGACCAGTGTGTTGCAGACAGAGAAGAAGCCTTTAAAGAA  
AAAGATGTTCAAAGACTTATGCGACAGATTTTAGAAGGTGTTCACTTTTTACACACTCGT  
GATGTAGTTCATCTTGATTTGAAGCCTCAGAATATTCTGTTGACAAGTGAATCTCCATTG  
GGTGACATTAAGATTGTTGATTTTGGCCTTTCAAGAATATTGAAGAACAGTGAAGAGCTC  
CGAGAAATTATGGGTACCCCTGAATATGTGGCTCCTGAAATTCTTAGTTATGATCCTATA  
AGCATGGCAACAGATATGTGGAGCATTGGAGTGTTAACATATGTCATGCTTACAGGAATA  
TCACCTTTCTTAGGCAATGATAAACAAGAAACATTCTTAAACATCTCACAGATGAATTTA  
AGTTATTCTGAGGAAGAATTTGATGTTTTGTCTGAGTCGGCTGTTGATTTTCATCAGGACA  
CTTTTAGTTAAGAAACCTGAAGATCGAGCCACTGCTGAAGAATGTCTAAAGCACCCCTGG  
TTGACACAGAGCAGTATTCAAGAGCCTTCTTTCAGGATGGAAAAGGCACTAGAAGAAGCA  
AATGCCCTCCAAGAAGGTCATTCTGTGCCTGAAATTAATTCGGATACCGACAAATCAGAA  
AATCGAGGAATCCATTGTAACCGAAGAGTTAATTGTAGTTACTTCATATACTCTAGGACAA  
TGCAGACAGTCTGAAAAAGAGAAAATGGAGCAAAAGGCCATTTCCAAACGATTTAAATTT  
GAGGAACCTTTGCTACAAGAAATTCCAGGAGAATTTATCTACTGA

SEQ ID NO: 32\_AA021445\_H

CGGGGCTGCCGGGGCGGGACTGGGGGAGCCGGGGCCCGCGGGCCCGCCTGCTGCCTCCGCC  
CGCGCCGGGGTCCCCAGCCGCCCGCGCTGCCGTGTCCCCTGCGGGCCGGCCAGCCGCGTCC  
CCCAGCCCCGGCCTCCCGCGGACCCATGCCCGCCCGTATCGGCTACTACGAGATCGACCG  
CACCATCGGCAAGGGCAACTTCGCGGTGGTCAAGCGGGCCACGCACCTCGTCACCAAGGC  
CAAGGTTGCTATCAAGATCATAGATAAGACCCAGCTGGATGAAGAAAACCTGAAGAAGAT  
TTTCCGGGAAGTTCAAATTATGAAGATGCTTTGCCACCCCCATATCATCAGGCTCTACCA  
GGTTATGGAGACAGAACGGATGATTTATCTGGTGACAGAATATGCTAGTGGAGGGGAAAT  
ATTTGACCACCTGGTGGCCCATGGTAGAATGGCAGAAAAGGAGGCACGTCGGAAGTTCAA  
ACAGATCGTCACAGCTGTCTATTTTTGTCACTGTCGGAACATTGTTTCATCGTGATTTAAA  
AGCTGAAAATTTACTTCTGGATGCCAATCTGAATATCAAAATAGCAGATTTTGGTTTCAG  
TAACCTCTTCACTCCTGGGCAGCTGCTGAAGACCTGGTGTGGCAGCCCTCCCTATGCTGC  
ACCTGAACTCTTTGAAGGAAAAGAATATGATGGGCCCCAAAGTGGACATCTGGAGCCTTGG  
AGTTGTCTCTACGTGCTTGTGTGCGGTGCCCTGCCATTTGATGGAAGCACACTGCAGAA  
TCTGCGGGCCCGCGTGCTGAGTGGAAAGTTCGCGCATCCCATTTTTTATGTCCACAGAATG  
TGAGCATTTGATCCGCCATATGTTGGTGTAGATCCCAATAAGCGCCTCTCCATGGAGCA  
GATCTGCAAGCACAAAGTGGATGAAGCTAGGGGACGCCGATCCCAACTTTGACAGGTTAAT  
AGCTGAATGCCAACAACCTAAAGGAAGAAAGACAGGTGGACCCCTGAATGAGGATGTCTT  
CTTGGCCATGGAGGACATGGGACTGGACAAAGAACAGACACTGCAGTCATTAAGATCAGA

## FIGURE 2W

TGCCTATGATCACTATAGTGCAATCTACAGCCTGCTGTGTGATCGACATAAGAGACATAA  
AACCTTGGCTCTCGGAGCACTTCCTAGCATGCCCCGAGCCCTGGCCTTTCAAGCACCACT  
CAATATCCAGGCGGAGCAGGCAGGTACTGCTATGAACATCAGCGTTCCCCAGGTGCAGCT  
GATCAACCCAGAGAACCAAATTGTGGAGCCGGATGGGACACTGAATTTGGACAGTGATGA  
GGGTGAAGAGCCTTCCCCCTGAAGCATTGGTGCGCTATTTGTCAATGAGGAGGCACACAGT  
GGGTGTGGCTGACCCACGCACGGAAGTTATGGAAGATCTGCAGAAGCTCCTACCTGGCTT  
TCCTGGAGTCAACCCCCAGGCTCCATTCTCTGCAGGTGGCCCCCTAATGTGAACTTCATGCA  
CAACCTGTTGCCTATGCAAACTTGCAACCAACCGGGCAACTTGAGTACAAGGAGCAGTC  
TCTCCTACAGCCGCCACGCTACAGCTGTTGAATGGAATGGGCCCCCTTGGCCGGAGGGC  
ATCAGATGGAGGAGCCAACATCCAACCTGCATGCCCAGCAGCTGCTGAAGCGCCACGGGG  
ACCTCTCCGCTTGTACCATGACACCAGCAGTGCCAGCAGTTACCCCTGTGGACGAGGA  
GAGCTCAGACGGGGAGCCAGACCAGGAAGCTGTGCAGAGGTACTTGGCAAATAGGTCCAA  
AAGACATACTGGCCATGACCAACCTACAGCTGAGATCCCACCGGACCTACAACGGCA  
GCTAGGACAGCAGCCTTTCCGTTCCCGGGTCTGGCCTCCTCACCTGGTACCTGATCAGCA  
TCGCTCTACCTACAAGGACTCCAACACTCTGCACCTCCCTACGGAGCGTTTCTCCCCTGT  
GCGCCGGTTCTCAGATGGGGCTGCGAGCATCCAGGCCTTCAAAGCTCACCTGGAAAAAAT  
GGGCAACAACAGCAGCATCAAACAGCTGCAGCAGGAGTGTGAGCAGCTGCAGAAGATGTA  
CGGGGGGCGAGATTGATGAAAGAACCCTGGAGAAGACCCAGCAGCAGCATATGTTATACCA  
GCAGGAGCAGCACCATCAAATTCTCCAGCAACAAATTCAAGACTCTATCTGTCCTCCTCA  
GCCATCTCCACCTCTTCAGGCTGCATGTGAAAATCAGCCAGCCCTCCTTACCCATCAGCT  
CCAGAGGTTAAGGATTCAGCCTTCAAGCCCACCCCCCAACCACCCCAACAACCATCTCTT  
CAGGCAGCCCAGTAATAGTCCTCCCCCATGAGCAGTGCCATGATCCAGCCTCACGGGGC  
TGCATCTTCTTCCCAGTTTCAAGGCTTACCTTCCCGCAGTGCAATCTTTCAGCAGCAACC  
TGAGAACTGTTCTCTCCTCCCAACGTGGCACTAACCTGCTTGGGTATGCAGCAGCCTGC  
TCAGTCACAGCAGGTCACCATCCAAGTCCAAGAGCCTGTTGACATGCTCAGCAACATGCC  
AGGCACAGCTGCAGGCTCCAGTGGGCGCGGCATCTCCATCAGCCCCAGTGCTGGTCAGAT  
GCAGATGCAGCACCGTACCAACCTGATGGCCACCCTCAGCTATGGGCACCGTCCCTTGTC  
CAAGCAGCTGAGTGCTGACAGTGCAGAGGCTCACAGCTTGAACGTGAATCGGTTCTCCCC  
TGCTAACTACGACCAGGCGCATTTACACCCCCATCTGTTTTTCGGACCAGTCCCGGGGTTC  
CCCCAGCAGCTACAGCCCTTCAACAGGAGTGGGGTTCTCTCCAACCCAAGCCCTGAAAGT  
CCCTCCACTTGACCAATTCCCCACCTTCCCTCCCAGTGCACATCAGCAGCCGCCACACTA  
TACCACGTCGGCACTACAGCAGGCCCCTGCTGTCTCCCACGCCGCCAGACTATACAAGACA  
CCAGCAGGTACCCACATCCTTCAAGGACTGCTTTCTCCCCGGCATTCGCTCACCGGCCA  
CTCGGACATCCGGCTGCCCCCAACAGAGTTTGCACAGCTCATTAAGGAGCAGCAGCAACA  
ACGGCAGCAGCAGCAGCAACAGCAGCAACAGCAAGAATACCAGGAAGTGTTCAGGCACAT  
GAACCAAGGGGATGCGGGGAGTCTGGCTCCCAGCCTTGGGGGACAGAGCATGACAGAGCG  
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GTATGCTCACAGCCGGCACTGATGCATTACAGAGAGCATGGAGGAGGACTGCTCGTGTGA  
GGGGGCCAAGGATGGCTTCCAAGACAGTAAGAGTTCAAGTACATTGACCAAGGTTGCCA  
TGACAGCCCTCTGCTCTTGAGTACCGGTGGACCTGGGGACCCTGAATCTTTGCTAGGAAC  
TGTGAGTCATGCCCAAGAATTGGGGATACATCCCTATGGTCATCAGCCAACTGCTGCATT  
CAGTAAAAATAAGGTGCCCAGCAGAGAGCCTGTCATAGGGAACTGCATGGATAGAAGTTC  
TCCAGGACAAGCAGTGGAGCTGCCGGATCACAATGGGCTCGGGTACCCAGCACGCCCCCTC  
CGTCCATGAGCACACAGGCCCCGGGCCCTCCAGAGACACCACACGATCCAGAACAGCGA  
CGATGCTTATGTACAGCTGGATAACTTGCCAGGAATGAGTCTCGTGGCTGGGAAAGCACT  
TAGCTCTGCCCCGATGTCGGATGCAGTTCTCAGTCAGTCTTCGCTCATGGGCAGCCAGCA  
GTTTCAGGATGGGGAAAATGAGGAATGTGGGGCAAGCCTGGGAGGTCATGAGCACCCAGA  
CCTGAGTGATGGCAGCCAGCATTTAAACTCCTCTTGCTATCCATCTACGTGTATTACAGA  
CATTCTGCTCAGCTACAAGCACCCCGAAGTCTCCTTCAGCATGGAGCAGGCAGGCGTGTA

## FIGURE 2X

ACAAGAAACAGAGAGTTTTGTGTACAGCTTGGGAATGAAAAGGTTGATTGTAAACCCACA  
GTATCTAGCAGCGTTGTGCCAAATTGCCCTTGTGTTTCTCTCCACCCAAAATATCACAGC  
TGCTTTCCCTCACATTTGSTTCATCCGTGTGCTGTTCTTTTGGGTTCTGAGAGGGTTTTGC  
CATGTTTGCTTGTATGACCAAGTCACCAAGGAAATAAACAGGAAGGAAATCCATGTTCTC  
C

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CTGGGCCGCTGCCGGTCAGGTCGGGCCGCCCTGACAGCTCCGGGAGCCTCAAGCGCGACA  
GGGCGCCCTCACCTCGGGACATCCACACACCGACCGCTCCTGCTCCAGAGGCAACAACCC  
AGCGCGCCTAGCCTGGCGCCGTGCAGCGAAGCCCAAGAGCTGGCCTCGCCACGAAGGTTG  
AACCAGCCAAATTTTCGAGACAGCTCACGGCTTAGAGGAAGGTTTCATCTAAATAAAGGCC  
GGCTAAAGTGACATTGCAGGGATTAAATCCTTCTTTGGCTGCCTGTGTGACCAGAAGGCT  
TATTTGCAAGTTTCTTCTTTCCTGGGGTCCAGATTATTAGGTCTCCAGCGCCCTGCAGCT  
TGACAGAAAGAGAAGCATGAAATGAAGGTCAGAGATGAGATCCCGCAGCAGGGACGTGGG  
GGCCTCCCAGGGGCATTTACGCACCAGAGTGCAAGATTCTCTGGCCATCAAGGGGAAATAG  
CAAACAGAAGCCTTTGTCCTGGGGCACAGCCACCTACCACAAAGCATCAGACTCCACGTC  
TGGCCAGAAAGTTCTTGGAGTCCCATCAGGCCAGTGGGTATGTAACATGTGCCTAATTGT  
ACAGCTAGAGCCTGCAAGTTCAACGTGAGGGAAGGTGGGAAATGTCTTGAGTGAGGCGAG  
CAGCTCCTGGCTGGGCTGGGCAGACTCAGCTACCACGTTCACTGCCTTCTCTCACTAAA  
GCCGAGAGGGAGGCTGCTCAGCTCTCAGGAAAACCTTTTTGAACCCTGGGCACCTGCTGT  
CCTCAGTTGGCATCTCCACCCCTCTGAGCCTCTTCTGCTCCTGCACAACCTGCCTCTTCG  
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CTGGTGAACCCCCACTATGCCCGGTGGGATCGGCGCGACAGTGTAGAAAGTGGCTGTCAG  
ACCGAGAGTAGCAAGGAGGGTGAGGAGGGACAGCCCCGCCAGCTGACGCCCTTCGAGAAA  
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GACCAGAAAACCCAGAGGCTACTATCCCGAGAAATCTCCAGCATGGAAAAGCTGCACCAT  
CCCAACATCATCCGCCTTTACGAAGTGGTGGAGACCCTATCCAAGCTGCACTTGGTGATG  
GAGTATGCAGGGGGTGGGGAGCTCTTCGGAAAAATTAGCACTGAGGGGAAGCTCTCTGAA  
CCAGAAAGCAAGCTCATCTTCTCCAGATTGTGTCTGCCGTGAAGCACATGCATGAAAAC  
CAAATTATTATAGAGATCTGAAAGCAGAAAATGTATTCTATAACAGTAATACTTGTGTG  
AAGGTGGGCGATTTTGGATTTCAGCACAGTAAGCAAAAAAGGTGAAATGCTGAACACTTTC  
TGTGGGTCTCCTCCCTACGCTGCGCCTGAACTCTTCCGGGACGAGCACTACATCGGCATT  
TACGTGGATATCTGGGCCTTGGGGGTGCTTTTGTACTTCATGGTGACTGGCACCATGCCA  
TTTCGGGCAGAAACCGTGGCCAAACTAAAAAAGAGCATCCTCGAGGGGCACATACAGTGTA  
CCGCCGCACGTGTCAGAGCCCTGCCACCGACTCATCCGAGGAGTCCTTCAGCAGATCCCC  
ACGGAGAGGTACGGAATCGACTGCATCATGAATGATGAATGGATGCAAGGGGTGCCATAC  
CCTACACCTTTGGAACCTTTCCAACCTGGATCCCAACATTTGTCTGGAAACCAGCACTCTC  
AAGGAAGAAGAAAATGAGGTCAAAAGCACTTTAGAACATTTGGGCATTACAGAAGAGCAT  
ATTCGAAATAACCAAGGGAGAGATGCTCGCAGCTCAATCACAGGGGTCTATAGAATTATT  
TTACATAGAGTCCAAAGGAAGAAGGCTTTGGAAAGTGTCCTCAGTCATGATGCTACCAGAC  
CCTAAAGAAAGAGACCTCAAAAAAGGGTCCCGTGTCTACAGAGGGGATAAGACACACATCC  
AAATTTTGCTCGATTTTATAAATTGCACTAGACTGCTTGTAACCTAACCAAGATGATTGTT  
GCTGCTTCTAAATTTTTTTTCAAGGACAACCTTGAGTGGAGACATTTTTTGTAATTTTTTAAAT  
AAACTTAAATTTGAGATATGCAAAAAA

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ATGTCCACTAGGACCCCATTTGCCAACGGTGAATGAACGAGACACTGAAAACCACACGTCA  
CATGGAGATGGGCGTCAAGAAGTTACCTCTCGTACCAGCCGCTCAGGAGCTCGGTGTAGA



## FIGURE 2Y

AACTCTATAGCCTCCTGTGCAGATGAACAACCTCACATCGGAAACTACAGACTGTTGAAA  
ACAATCGGCAAGGGGAATTTTGCAAAAGTAAAATTGGCAAGACATATCCTTACAGGCAGA  
GAGGTTGCAATAAAAAATAATTGACAAAACCTCAGTTGAATCCAACAAGTCTACAAAAGCTC  
TTCAGAGAAGTAAGAATAATGAAGATTTTAAATCATCCCAATATAGTGAAGTTATTGAA  
GTCATTGAAACTGAAAAAACACTCTACCTAATCATGGAATATGCAAGTGGAGGTGAAGTA  
TTTGACTATTTGGTTGCACATGGCAGGATGAAGGAAAAAGAAGCAAGATCTAAATTTAGA  
CAGATTGTGTCTGCAGTTCAATACTGCCATCAGAAACGGATCGTACATCGAGACCTCAAG  
GCTGAAAATCTATTGTTAGATGCCGATATGAACATTAAAAATAGCAGATTTTCGGTTTTAGC  
AATGAATTTACTGTTGGCGGTAAACTCGACACGTTTTTGTGGCAGTCCTCCATACGCAGCA  
CCTGAGCTCTTCCAGGGCAAGAAATATGACGGGGCCAGAAGTGGATGTGTGGAGTCTGGGG  
GTCATTTTATACACACTAGTCAGTGGCTCACTTCCCTTTGATGGGCAAAACCTAAAGGAA  
CTGAGAGAGAGAGTATTAAGAGGGGAAATACAGAATTCCTTCTACATGTCTACAGACTGT  
GAAAACCTTCTCAAACGTTTCTTGGTGCTAAATCCAATTAAACGCGGCACTCTAGAGCAA  
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AATCTTTCACTTGCTAAGGTTAGGCCGAGCAGTGATCTCAACAACAGTACTGGCCAGTCT  
CCTCACCAAAAGTGCAGAGAAGTGTTTCTTCAAGCCAAAAGCAAAGACGCTACAGTGAC  
CATGCTGGACCAGCTATTCCTTCTGTTGTGGCGTATCCGAAAAGGAGTCAGACAAGCACT  
GCAGATGGTGACCTCAAAGAAGATGGAATTTCTTCCCGGAAATCAAGTGGCAGTGCTGTT  
GGAGGAAAGGGAATTGCTCCAGCCAGTCCCATGCTTGGGAATGCAAGTAATCCTAATAAG  
GCGGATATTCCTGAACGCAAGAAAAGCTCCACTGTCCCTAGTAGTAACACAGCATCTGGT  
GGAATGACACGACGAAATACTTATGTTTGCAGTGAGAGAACTACAGCTGATAGACACTCA  
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ACACACAGTATCAGTAGTGCAGCCACCCCAGATCGAATCCGCTTCCCAAGAGGCACTGCC  
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CCTGCCTCTCCCAGCCTGTCCCATGAAGCCACACCATTGTCCCAGACTCGAAGCCGAGGC  
TCCACTAATCTCTTTAGTAAATTAACCTTCAAACTCACAAGGAGTCGCAATGTATCTGCT  
GAGCAAAAAGATGAAAACAAAGAAGCAAAGCCTCGATCCCTACGCTTCACCTGGAGCATG  
AAAACCACTAGTTCAATGGATCCCGGGGACATGATGCGGGAAATCCGCAAAGTGTTGGAC  
GCCAATAACTGCGACTATGAGCAGAGGGAGCGCTTCTTGCTCTTCTGCGTCCACGGAGAT  
GGGCACGCGGAGAACCCTCGTGCAGTGGGAAATGGAAGTGTGCAAGCTGCCAAGACTGTCT  
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TCCAAAATTGCCAATGAGCTAAAGCTGTAA

SEQ ID NO: 35\_W90839\_M

AAAGGGCCGTCCTGGTCCAGCCGTTCCCTGGGTGCCCCGTTGCCGGAACCTCTATCGCTTCC  
TGCCCTGAGGAACAACCCCATGTGGGCAACTATAGGCTGCTAAGGACCATCGGGAAGGGC  
AACTTCGCCAAAGTCAAGCTGGCTCGGCATATCCTCACGGGGCCGGGAGGTCTGCTATTAAG  
ATCATTGATAAGACCCAGCTGAACCCCAAGTAGCTTGCAGAAGCTGTTTCAGAGAAGTCCGA  
ATTATGAAGGGACTCAACCACCCCAACATCGTGAAGCTTTTTTGAGGTGATAGAGACGGAG  
AAGACGCTATACCTGGTGATGGAATACGCTAGCGCAGGAGAAGTGTTTGACTACCTCGTG  
TCGCACGGCCGCATGAAGGAGAAGGAGGCTCGAGCCAAGTTCCGGCAGATCGTGTCAGCC  
GTGCACTACTGTCATCAGAAGAACATTGTACACAGGGATCTAAAGGCTGAAAACCTGTTG  
CTGGATGCCGAGGCCAACATCAAAATCGCCGACTTCGGCTTCAGCAATGAGTTCACGCTG  
GGCTCCAAGCTGGACACCTTCTGTGGGAGCCCCCATAACGCCGCCCCAGAGCTGTTCCAG  
GGCAAGAAGTATGATGGGCCAGAGGTGGACATCTGGAGCCTGGGTGTCTATCCTGTACACG  
CTGGTCAGCGGCTCCCTGCCCTTCGATGGGCACAACCTCAAGGAGCTGCGGGAGCGAGTC  
CTCAGAGGAAAGTACCGGGTCCCCTTCTACATGTCTACAGACTGCGAGAGCATTCTGCGG

## FIGURE 27

AGATTTCTGGTGCTGAACCCCGCAAAACGCTGTACTCTGGAGCAAATCATGAAAGACAAA  
TGGATCAACATCGGCTATGAGGGTGAGGAGCTGAAGCCAGACACGGAGCTCAAAGAAGAG  
CGGATGCCGGGTCCGAAAGCGAGCTGCAGTGCAGTGGGCAGTGGAAAGTCGAGGCTTGCCC  
CCCTCCAGCCCCATGGTCAGCAGTGCCCCACAACCCCAATAAGGCAGAGATCCCTGAGCGG  
CGGAAGGACAGCACTAGCACCCCTAACAACCTCCCCCCCCAGCATGATGACCCGAAGAAAC  
ACCTATGTGTGCACAGAGCGACCAGGATCTGAACGCCCGTCCTTGTTGCCAAATGGCAAA  
GAAAATAGCTCCGGTACCTCGCGGGTGCCCCCTGCCTCGCCTTCCAGTCATAGCCTGGCT  
CCCCCGTCAGGCGAGCGGAGCCGCTGGCTCGGGGCTCCACCATCCGCAGCACCTTCCAT  
GGGGGCCAGGTCCGAGACCGGCGGGCAGGGAGCGGGAGTGGCGGGGGTGTGCAGAATGGA  
CCCCCAGCCTCACCCACGCTTGCCCCACGAGGCCGACCCCTGCCCTCCGGGCGGCCTCGC  
CCCACCACCAACCTCTTCACCAAGCTGACCTCCAAACTGACCCGAAGGGTCCACAGACGAA  
CCTGAGAGAATCGGGGGACCTGAGGTCACAAGTTGCCATCTACCTTGGGATAAAACGGAA  
ACCGCCCCCAGGCTGCTCCGATTCCCCTGGAGTGTGAAGCTGACCAGCTCGCGACCTTCC  
TGAGGCCCTGATGGCTGCCCTGCGACAGGCCACA

SEQ ID NO: 36\_406786.5\_H

GTAGCCGGCTTGCGGTGACCGTCGCCTGATCCAGTTGTTAGAGGTGGAAGCTTGGCAGTT  
GGCCTCCCTTCTTCCCATGGAGGTGCGGGGGCTTAACAGTCTTTGAAGAGGACCAGAGATG  
CCTTTCCCAGAGCCTCCCCTTGCCAGTGTGAGCAGAGGGGCCAGCTGCACAGACCACTGC  
TGAGCCCAGCAGGTGCTTTTCTCTCAGCCCACAGACACCTGAGCAGAAGGAATGGGCTTTC  
CAGACTCTGCCAGAGCAGGACGGCGCTCTCTGAAGACAGATGGAGCTCCTATTGTCTATC  
ATCACTGGCTGCCCAGAATATTTGTACAAGTAAACTGCACTGCCCTGCTGCCCCCTGAGCA  
CACGGACCCGTCCGAACCGCGGGGGCAGTGTGTCTCTGCTGCTCCCTGCTGCGGGGACTGTC  
CTCAGGGTGGTCCTCACCTCTGCTTCCGGCCCCCTGTGTGCAACCCTAACAAGGCCATCTT  
CACGGTGGATGCCAAGACCACAGAGATCCTCGTTGCTAACGACAAAGCTTGCGGGCTCCT  
GGGGTACAGCAGCCAGGACCTGATTGGCCAGAAGCTCACGCAGTTCTTTCTGAGGTCAGA  
TTCTGATGTGGTGGAGGCCCTCAGCGAGGAGCACATGGAGGCCGACGGCCACGCTGCGGT  
GGTGTTTGGCACGGTGGTGGACATCATCACCCGTAGTGGGGAGAAGATTCCAGTGTCTGT  
GTGGATGAAGAGGATGCGGCAGGAGCGCCGCTATGCTGCGTGGTGGTCCTGGAGCCCGT  
GGAGAGGGTCTCGACCTGGGTGCTTTCCAGAGCGATGGCACCATCACGTCATGTGACAG  
TCTCTTTGCTCATCTTCACGGGTACGTGTCTGGGGAGGACGTGGCTGGGCAGCATATCAC  
AGACCTGATCCCTTCTGTGCAGCTCCCTCCTTCTGGCCAGCACATCCCAAAGAATCTCAA  
GATTCAGAGGTCTGTTGGAAGAGCCAGGGACGGTACCACCTTCCCTCTGAGCTTAAAGCT  
GAAATCCCAACCCAGCAGCGAGGAGGCGACCACCGGTGAGGCGGCCCTGTGAGCGGCTA  
CCGGGCATCTGTCTGGGTGTTCTGCACCATCAGTGGCCTCATCACCTCCTGCCGGATGG  
GACCATCCACGGCATCAACCACAGCTTCGCGCTGACACTGTTTGGTTACGGAAAGACGGA  
GCTCCTGGGCAAGAATATCACTTTCCTGATTCTTGGTTTCTACAGCTACATGGACCTTGC  
GTACAACAGCTCATTACAGCTCCCAGACCTGGCCAGCTGCCTGGACGTCGGCAATGAGAG  
TGGGTGTGGGGAGAGAACCTTGGACCCGTGGCAGGGGCCAGGACCCAGCTGAGGGGGGCCA  
GGATCCAAGGATTAATGTCGTGCTTGCTGGTGGCCACGTTGTGCCCCGAGATGAGATCCG  
GAAGCTGATGGAAAGCCAAGACATCTTCACCGGGACTCAGACTGAGCTGATTGCTGGAGG  
CCAGCTCCTTTCCTGCCTCTCACCTCAGCCTGCTCCAGGGGTGGACAATGTCCCAGAAGG  
AAGCCTGCCAGTGCACGGTGAACAGGCGCTGCCCAAGGACCAGCAAATCACTGCCTTGGG  
GAGAGAGGAACCTGTGGCAATAGAGAGCCCCGGACAGGATCTTCTGGGAGAAAGCAGGTC  
TGAACCAGTGGATGTGAAGCCATTTGCTTCCTGCGAAGATTCTGAAGCTCCAGTCCCAGC  
TGAGGATGGGGGCAGTGATGCTGGCATGTGTGGCCTGTGTGAGAAGGCCAGCTAGAGCG  
GATGGGAGTCAGTGGTCCCAGCGGTTTACAGACCTTTGGGCTGGGGCTGCCGTGGCCAAGCC  
CCAGGCCAAGGGTCAGCTGGCGGGGGGCGAGCCTCCTGATGCACTGCCCTTGCTATGGGAG  
TGAATGGGGCTTGTGGTGGCGAAGCCAGGACTTGGCCCCCAGCCCCCTCTGGGATGGCAGG  
CCTCTCGTTTGGGACACCTACTCTAGATGAGCCGTGGCTGGGAGTGGAAAACGACCGAGA



## FIGURE 2AA

AGAGCTGCAGACCTGCTTGATTAAGGAGCAGCTGTCCCAGTTGAGCCTTGCAGGAGCCCT  
GGATGTCCCCCACGCCGAACCTCGTTCCGACAGAGTGCCAGGCTGTCACCGCTCCTGTGTC  
GTCCTGCGATCTGGGAGGCAGAGACCTGTGCGGTGGCTGCACGGGCAGCTCCTCAGCCTG  
CTATGCCTTGGCCACGGACCTCCCTGGGGGCCTGGAAGCAGTGGAGGGCCAGGAGGTGA  
TGTGAATTTCGTTTTCTGGAACCTCAAGGAACTCTTTTTCAGTGACCAGACAGACCAAAC  
GTCATCAAATTGTTCTGTGCTACGTCTGAACTCAGAGAGACACCCTCTTCCTTGGCAGT  
GGGCTCCGATCCAGATGTAGGCAGTCTCCAGGAACAGGGGTGCTGTGTCCTGGATGACAG  
GGAGCTGTTACTACTGACCGGCACCTGTGTTGACCTTGGCCAAGGCCGACGGTTCCGGGA  
GAGCTGTGTGGGACATGATCCAACAGAACCGCTTGAGGTTTGTGTTGGTGTCTCTGAGCA  
TTATGCAGCAAGCGACAGAGAAAGCCCAGGACACGTTCCCTCCACGTTGGATGCTGGCCC  
TGAGGACACGTGCCCATCAGCAGAGGAGCCAAGGCTGAACGTCCAGGTACCTCCACGCC  
CGTGATCGTGATGCGCGGGGCTGCTGGCCTGCAGCGGGAGATCCAGGAGGGTGCTACTC  
CGGGAGCTGCTACCATCGAGATGGCTTACGGCTGAGTATACAGTTTGAGGTGAGGCGGGT  
GGAGCTCCAGGGCCCCACACCTCTGTTCTGCTGCTGGCTGGTGAAAGACCTCCTCCACAG  
CCAACGCGACTCAGCCGCCAGGACCCGCCCTGTTCTTGCCAGCCTGCCCGGCTCCACCCA  
CTCTACCGCTGCTGAGCTCACCGGACCCAGCCTGGTGGAAGTGCTCAGAGCCAGACCTG  
GTTTGAGGAGCCCCCAAGGCTGTGGAACCTGGAGGGGTGGCGGCCTGTGAGGGCGAGTA  
CTCCCAAAGTACAGTACCATGAGCCCGCTGGGCAGTGGGGCCTTCGGCTTCGTGTGGAC  
TGCTGTGGACAAGGGAAAAACAAGGAGGTGGTGGTGAAGTTTATTAAGAAGGAGAAGGT  
CTTGAGGATTGTTGGATTGAGGATCCCAAACCTTGGGAAAGTTACTTTAGAGATCGCAAT  
TCTATCCAGGGTGGAGCACGCCAATATCATCAAGGTATTGGATATATTTGAAAACCAAGG  
GTTCTTCCAGCTTGTGATGGAGAAGCACGGCTCCGGCCTAGACCTCTTCGCTTTCATCGA  
CCGCCACCCAGGCTGGATGAGCCCTGGCGAGCTACATCTTCCGACAAGTGAGAGCAGG  
CCAGAGCCGTCTAGTGTCAGCAGTGGGATACCTGCGCTTGAAGGACATCATCCACCGTGA  
CATCAAGGATGAGAACATCGTGATCGCTGAGGACTTCACAATCAAGCTGATAGACTTTGG  
CTCGGCCGCCTACTTGGAAGGGGAAAATTATTTTATACTTTTTGTGGGACCATCGAGTA  
CTGTGCACCGGAAGTTCTCATGGGGAATCCCTACAGAGGGCCCGGAGCTGGAGATGTGGTC  
TCTGGGAGTCACTCTGTACACGCTGGTCTTTGAGGAGAACCCTTCTGTGAGCTGGAGGA  
GACCGTGGAGGCTGCCATACACCCGCCATACCTGGTGTCCAAAGAACTCATGAGCCTTGT  
GTCTGGGCTGCTGCAGCCAGTCCCTGAGAGACGCACCACCTTGGAGAAGCTGGTGACAGA  
CCCGTGGGTAAACACAGCCTGTGAATCTTGCTGACTATACATGGGAAGAGGTGTTTCGAGT  
AAACAAGCCAGAAAGTGGAGTTCTGTCCGCTGCGAGCCTGGAGATGGGGAAACAGGAGCCT  
GAGTGATGTGGCCCAGGCTCAGGAGCTTTGTGGGGGGCCCCGTTCCAGGCGAGGCTCCTAA  
TGGCCAAGGCTGTTTGCATCCCGGGGATCCCCGTCTGCTGACCAGCTAAACACCAATTTT  
TTCCTGCTTTTCTCCACTTGGTTTGGAAAATCACACAGTTTTTCAGGCTCCATCTGTTTG

SEQ ID NO: 37\_AA544838\_M 406786\_M

CCACGCGTCCGCATCCCTGCTTGATGAGCCCCTGGCGAGTTTCATCTTTTCGACAACTAG  
TGTCTGCTGTAGGATACCTGCACTCCCAAGGCATCATCCATAGAGACATCAAGGATGAGA  
ACATTGTGATTGCTGAGGACTTCACAATTAAGCTGATAGATTTTGGCTCAGCTGCCTACT  
TAGAGAGGGGGCAAACCTATTTTATACCTTTTGTGGAACAATCGAATACTGTGCACCTGAGG  
TTCTCATTTGGAAATCCCTACAGAGGGCCAGAGCTGGAGATGTGGTCTCTGGGGGTACCCC  
TGTACACGCTCATCTTCGAGGAGAATCCCTTCTGTGAGGTGGAGGAGACCATGGAGGCAG  
TTATTCATCCCCCATTCCTGGTTTCCCAAGAACTTATGAGTCTTCTGTCTGGACTGCTGC  
AGCCTTGCCCTGAGCAGCGGACCACTTTGGAGAAGCTGATCAGGGACCCCTGGGTGACAC  
AGCCTGTGAACCTTGCTAGCTATACTTGGGAAGAGGTGTGTAGGACCAACCAGCCAGAAA  
GTGGCCTGCTGTGAGCTGCAAGTCTGGAGATTGGGAGTAGGAGTCCAAGTGAAATGGCTC  
AGAGAGAGGGTCTCTGTGGGCCTCCTGCTCCCAGGGAGACTCGTGCTGACCAGCACTGCT  
TGCATCTTAAGGACCCCTCTTTGCCAGTCAGCTGAGCAAGCTCTCCTGCTCTTTGGTTTG  
GGCAGTTGTATGGATTTTCAGGGCTTTCTACCTGGAGAAAGGAAGTTGTGAAGGATTGGGA

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## FIGURE 2BB

TGACTTCTGCTTCTAGATTCTATGCAAATGCTACAAGAGCCTGCGATGCTAGTTTTCTT  
AGGTTTATGATATAGACTTGTAATTCATGTTTTTTTTTATAACCTTGAAAATCATTCTAATG  
TTCAGTTATACTGTACTATTAAAGGGCTTTAAGTTGTAAGCCTCAGAAAGACACAAGGAG  
TGTTTAAGTTCTCTATTTTTTGTTGTTTGTGTTTTGCTTGTAAGTTTTTGAGACAGGATCTC  
ACCATGTAACCTTGGCTGGCCTGGAACCTCAACTATGTAGACCAGGTAGACCTTAAACTGA  
CAGATCTGCCTGCGCTTGCCTCCCAAGCATTAGGACTGATGGTGTGTGTCAACCATGCCCA  
GTTCTTCTGTTTGTGTGTAGGTTTCTTTCCCACTGACTTGGTACATGTGACATGTGA  
CAGATGTATGGAGTCTATAGAAGTGGCCAGACAAAAATGGCCAGAATATTTATTTATTTT  
CTTAAAAATTTTCCAAATTAAAGCTACTTAGTTAACAGTTAAACTGGCCAGGACTATATG  
AGATAAACTTGGTTTTCTATTTCTTTTTGT

SEQ ID NO: 38\_AA785735\_H

GGCACGAGGCGCGCCTGGCTGGGCCCCTGCGGAGGANGGGAAGGAGCGAAGGAGCGAAGGA  
GCAAGCGGAGCGCAGTTGCCCCAAGCCAAGCCGCGCTGCCAACCTCCCGCCCCGCCGCG  
CTCCTGTCCGCCGTGTCTAGCAGCGGGGCCAGCATGGTCATGGCGGATGGCCCCGAGGCA  
CTTGACGCGCGGGCCGGTCCGGGTGGGGTTCTACGACATCGAGGGCACGCTGGGCAAGGG  
CAACTTCGCTGTGGTGAAGCTGGGGCGGCACCGGATCACCAAGACGGAGGTGGCAATAAA  
AATAATCGATAAGTCTCAGCTGGATGCAGTGAACCTTGAGAAAATCTACCGAGAAGTACA  
AATAATGAAAATGTTAGACCACCCTCACATAATCAAACCTTTATCAGGTAATGGAGACCAA  
AAGTATGTTGTACCTTGTGACAGAATATGCCAAAAATGGAGAAATTTTTGACTATCTTGC  
TAATCATGGCCGGTTAAATGAGTCTGAAGCCAGGCGAAAATTTCTGGCAAATCCTGTCTGC  
TGTTGATTATTGTCATGGTCGGAAGATTGTGCACCGTGACCTCAAAGCTGAAAATCTCCT  
GCTGGATAACAACATGAATATCAAATAGCAGATTTCCGGTTTTGGAAATTTCTTTAAAAG  
TGGTGAACCTGCTGGCAACATGGTGTGGCAGCCCCCTTATGCAGCCCCAGAAGTCTTTGA  
AGGGCAGCAGTATGAAGGACCACAGCTGGACATCTGGAGTATGGGAGTTGTTCTTTATGT  
CCTTGTCTGTGGAGCTCTGCCCTTTGATGGACCGACTCTTCCAATTTTGAGGCAGAGGGT  
TCTGGAAGGAAGATTCCGGATTCCGTATTTTCATGTCAGAAGATTGCGAGCACCTTATCCG  
AAGGATGTTGGTCTAGACCCATCCAAACGGCTAACCATAGCCCCAAATCAAGGAGCATAA  
ATGGATGCTCATAGAAGTTCCTGTCCAGAGACCTGTTCTCTATCCACAAGAGCAAGAAAA  
TGAGCCATCCATCGGGGAGTTTAATGAGCAGGTTCTGCGACTGATGCACAGCCTTGGAAAT  
AGATCAGCAGAAARCCATTGAGTCTTTGCAGAACAAAGAGCTATAACCACTTTGCTGCCAT  
TTATTTCTTGTGTTGGTGGAGCGCCTGAAATCACATCGGAGCAGTTTCCCAGTGGAGCAGAG  
ACTTGATGGCCGCCAGCGTCGGCCTAGCACCATTTGCTGAGCAAACAGTTGCCAAGGCACA  
GACTGTGGGGCTCCCAGTGACCATGCATTCACCGAACATGAGGCTGCTGCGATCTGCCCT  
CCTCCCCCAGGCATCCAACGTGGAGGCCTTTTCATTTCCAGCATCTGGCTGTCAGGCGGA  
AGCTGCATTCATGGAAGAAGAGTGTGTGGACACTCCAAAGGTCAATGGCTGTCTGCTTGA  
CCCTGTGCCTCCTGTCCTGGTGCAGGAAGGGATGCCAGTCACTGCCCAGCAACATGATGGA  
GACCTCCATTGACGAAGGGCTGGAGACAGAAGGAGAGGGCCGAGGAAGACCCCGCTCATGC  
CTTTGAGGCATTTTCAGTCCACACGCAGCGGGCAGAGACGGCACACTCTGTCAGAAGTGAC  
CAATCAACTGGTCGTGATGCCTGGGGCAGGGGAAAATTTTCTCCATGAATGACAGCCCCCTC  
CCTTGACAGTGTGGACTCTGAGTATGATATGGGGTCTGTTTCAGAGGGACCTGAACTTTCT  
GGAAGACAACCCTTCCCTTAAGGACATCATGTTAGCCAATCAGCCTTCACCCCGCATGAC  
ATCTCCCTTCATAAGCCTGAGACCTACCAACCCAGCCATGCAGGCTCTGAGCTCCCAGAA  
ACGAGAGGTCCACAACAGGTCTCCAGTGAGCTTCAGAGAGGGCCGAGAGCATCAGATAC  
CTCCCTCACCCAGGGAATTGTAGCATTTAGACAACATCTTCAGAATCTGGCTAGAACCAA  
AGGAATTCTAGAGTTGAACAAAGTGCAAGTTGTTGTATGAACAAATAGGACCGGAGGCAGA  
CCCTAACCTGGCGCCGGCGGCTCCTCAGCTCCAGGACCTTGCTAGCAGCTGCCCTCAGGA  
AGAAGTTTCTCAGCAGCAGGAAAGCGTCTCCACTCTCCCTGCCAGCGTGCATCCCCAGCT  
GTCCCCACGGCAGAGCCTGGAGACCCAGTACCTGCAGCACAGACTCCAGAAGCCCAGCCT  
TCTGTCAAAGGCCAGAACACCTGTCAGCTTTATTGCAAAGAACCACCGCGGAGCCTTGA

## FIGURE 2CC

GCAGCAGCTGCAGGAACATAGGCTCCAGCAGAAGCGACTCTTTCTTCAGAAGCAGTCTCA  
ACTGCAGGCCTATTTTAATCAGATGCAGATAGCAGAGAGCTCCTACCCACAGCCAAGTCA  
GCAGCTGCCCCCTTCCCCGCCAGGAGACTCCACCGCCTTCTCAGCAGGCCCCACCGTTTCA  
CCTGACCCAGCCCCCTGAGCCCCGTCTGGAGCCTTCCCTCCGAGCAGATGCAATACAGCCC  
TTTCCTCAGCCAGTACCAAGAGATGCAGCTTCAGCCCCCTGCCCTCCACTTCCGGTCCCCG  
GGCTGCTCCTCCTCTGCCCCACGCAGCTACAGCAGCAGCAGCCGCCACCGCCACCACCCCC  
TCCACCACCACGACAGCCAGGAGCTGCCCCAGCCCCCTTACAGTTCTCCTATCAGACTTG  
TGAGCTGCCAAGCGCTGCTTCCCCTGCGCCAGACTATCCCACTCCCTGTCAGTATCCTGT  
GGATGGAGCCCAGCAGAGCGACCTAACGGGGGCCAGACTGTCCCAGAAGCCCAGGACTGCA  
AGAGGCCCCCTCCAGCTACGACCCACTAGCCCTCTCTGAGCTACCTGGACTCTTTGATTG  
TGAAATGCTAGACGCTGTGGATCCACAACACAACGGGTATGTCCTGGTGAATTAGTCTCA  
GCACAGGAATTGAGGTGGGTGAGGTGAAGGAAGAGTGTATGTTCCCTATTTTTTATTCCAGC  
CTTTTAAATTTAAAGCTTATTTTCTTGCCCTCTCCCTAACGGGGAGAAATCGAGCCACCC  
AACTGGAATCAGAGGGTCTGGCTGGGGTGGATGTTGCTTCCCTCCTGGTTCTGCCCCACCA  
CAAAGTTTTCTGTGGCAAGTGCTGGAACATAGTTGTAGGCTGAGGCAGGAGAATGGCGTG  
AACCCGGGAGGCGGAGCTTGCACTGAGCCAAGATCGTGCCACTGCACTCCAGCCTGGGCG  
ACTGAGCAAGACTCCACCTCAAAAAAAAAAAAAAAAAAGGACAAGAGCAGTATCATCTGCCTC  
TGTTTCTAAACTGGACAAAGAGATTTTCTTAAAGTTTCTATCATCTCCCTTCTGACAGGT  
TCTACAGTGTGGTCTGAAGCACCTGTAATGTCAGAGCCCTTGTCTGGCCCTTGGTGGCAG  
GTGAACGAAAGCAGTGGAGCCTCTCACCTTCCAGTAGCCTCTCACATTCTTATTTTACCA  
TTTTTGTCCTAATTAAGGTAGCCTAGCTGATTCTAGAAGACAGCCATCCTACGTGCACCC  
CCACCTTGTGTCCACATCTTCTCCAGGCAGGTTTCAACCTATCAGCAGACTCAGGCACAC  
ACTGGGGCACAGATAGAGAACCAGGCGGCAGCAGTGCTCGCAGACCCACCCAGGGAGAGC  
TGTGATGGGTTCTGCCCAGATACTCTGCTCGCCCCACCCACAAGGGAGCAATAGCTTATAT  
TTGTACATTAGTTTTTACCAAGCACTTTCTCTTCTAACCTCACAACAATTCTATGAAATT  
AGCTGGGGAGATACTGTCCTTATTTTTTACAGCTGAAGAAACCAAAGCTTTGGGAAGTTT  
GTGACTTCTCTGAGATCACAGCTGGTGATAGAAGGAGCTGGGACACGCGCTTGGGTTGAC  
TGGCTTCTGGTTTTTGGTTCTCTGGCTTCTAGTGCTGGAAGAAGCCCTCTCTTTCCCTTCT  
CTTTCCCTCAGTAGCATCTGACTCTTTTTTACATAAGCAAACAGCTGTATAAAACAAAGCCCCCA  
TTTTGGTCAAGCACAGGGTGAATGTGATATTGTTCCCACAACCTTATTCTCCACTCAACA  
GCCGCCTGGCTTTGGGGAAGAGGCCCGCCTTCAGGTGACAGTGCAGCTGTCCAGGTGGCCG  
TGCACTGAACCAGGCTGAGGGAGACAAAAACCCCGCAGACCCGCTGCCTTTCAGCGTCC  
AGTTAACTGCAGAAGTTTAGGCTCACCTCAAAGATGTCTAGTTTTTCCAAGTTACAATAC  
AGCAGTTTCCCTACAGAACACCCCTTCCCTCAATTGCCAAGGGGCGCATCGCACGGCATC  
AGGCCACCACTGCAGGCCAGCAGATTCCACCCAGGAACGGTCATGAACTCAGCCTTTGT  
CTCAACGAGGGGCGTAACATTTCTTACAGTCAAGCCCCATCAACTAGAAGTGCTTATTA  
CTTTTAGGATTAAAAAAGTAATAACAGACTTTGACTTAATACTCTGTCTTTTCAGAGGCA  
AAGTGGGTGGGTAGAGGGGAGCTTTAAAAATAGAAGTACAAAACAACATCCTGGAAACAT  
ATGACCCAGATGGAATAATGTCACATTTCCCAAGTGCAGATAATGGGCTGCTGCTGGCTC  
TGTGGTGTCTGTCTGCAGAAGATTTGCTCAGTCAAGGAAATTCAAGTGGTGAGACCTTTC  
CACCATGGGTGGTAAGAGAAACCTGCCTTCACCAAATCTCTGAAGGGGAAAGAAGTGGA  
GAGAAAGGTTTGCTTCACTTCGGGGACTGCAGTTTGAGAAATAAAAGGGATACAGAGATA  
TCTGCACTTTGTAGAAAGGGCAAGATTATTTGCTTATATCTGAAGGGAGGTGGGTGGTTT  
TGCTGGATGTTTGGTCTGAAAGAGTTACTTTTGATAAAGTTAATCTAATTGTAGTTATAT  
TTTCTGTGTGCTTTTTTTTTAATTACTAAGAAAAAAATTGGTGAGTTCAGTAGCTTTGGTA  
TTATGAGTGCAAATCATAATAGCTCCAATGTGAAAAAAAATCAAAAGTATAACTTGTC  
ACTTAATGTTAGAAAATTGCCTAAAATGCAGTGTAATAAATAATCTCTGTACCAAATAGT  
AATTTAAATGGGGTAATTTTCTGCAAGGAAAAATGTACTGTTTTTATGTTTCCAACCTCT  
TGA



## FIGURE 2DD

SEQ ID NO: 39\_AA207220\_H

GCTGTGGCTCCCCGTCCTGGTGCGGGACCTGTGCCCCGCGCTTCAGCCCTCCCCGCAAGC  
CTATTGATTCCCCTGCCGCCCTTGCTCCACCTCCTGCTCGCCATGGAGTCGCTGGTTTTT  
GCGCGGCGCTCCGGCCCCACTCCCTCGGCCGCAGAGCTAGCCCGGCGCTGGCGGAAGG  
CTGATCAAGTCGCCCCAAGCCCCCTAATGAAGAAGCAGGCGGTGAAGCGGCACCACCACAAG  
CACAACCTGCGGCACCGCTACGAGTTCCTGGAGACCCTGGGCAAAGGCACCTACGGGAAG  
GTGAAGAAGGCGCGGGAGAGCTCGGGGCGCCTGGTGGCCATCAAGTCAATCCGGAAGGAC  
AAAATCAAAGATGAGCAAGATCTGATGCACATACGGAGGGAGATTGAGATCATGTTCATCA  
CTCAACCACCCTCACATCATTGCCATCCATGAAGTGTTTGAGAACAGCAGCAAGATCGTG  
ATCGTCATGGAGTATGCCAGCCGGGGCGACCTTTATGACTACATCAGCGAGCGGCAGCAG  
CTCAGTGAGCGCGAAGCTAGGCATTTCTTCCGGCAGATCGTCTCTGCCGTGCACTATTGC  
CATCAGAACAGAGTTGTCCACCGAGATCTCAAGCTGGAGAACATCCTCTTGGATGCCAAT  
GGGAATATCAAGATTGCTGACTTCGGCCTCTCCAACCTCTACCATCAAGGCAAGTTCCTG  
CAGACATTCTGTGGGAGCCCCCTCTATGCCTCGCCAGAGATTGTCAATGGGAAGCCCTAC  
ACAGGCCCCAGAGGTGGACAGCTGGTCCCTGGGTGTTCTCCTCTACATCCTGGTGCATGGC  
ACCATGCCCTTTGATGGGCATGACCATAAGATCCTAGTGAAACAGATCAGCAACGGGGCC  
TACCGGGAGCCACCTAAACCCTCTGATTGCCTGNNTGGCCTGATCCGGTGGCTGTTGATG  
GTGAACCCACCCGCCGGGCCACCCTGGAGGATGTGGCCAGTCACTGGTGGGTCAACTGG  
GGCTACGCCACCCGAGTGGGAGAGCAGGAGGCTCCGCATGAGGGTGGGCACCCTGGCAGT  
GACTCTGCCCCGCGCCTCCATGGCTGACTGGCTCCGGCGTTCTCCCGCCCCCTCCTGGAG  
AATGGGGCCAAGGTGTGCAGCTTCTTCAAGCAGCATGCACCTGGTGGGGGAAGCACCACC  
CCTGGCCTGGAGCGCCAGCATTCGCTCAAGAAGTCCCGCAAGGAGAATGACATGGCCCAG  
TCTCTCCACAGTGACACGGCTGATGACACTGCCCATCGCCCTGGCAAGAGCAACCTCAAG  
CTGCCAAAGGGCATTCTCAAGAAGAAGGTGTCAGCCTCTGCAGAAGGGGTACAGGAGGAC  
CCTCCGGAGCTCAGCCCAATCCCTGCGAGCCCAGGGCAGGCTGCCCCCTGCTCCCCAAG  
AAGGGCATTCTCAAGAAGCCCCGACAGCGCGAGTCTGGCTACTACTCCTCTCCCGAGCCC  
AGTGAATCTGGGGAGCTCTTGGACGCAGGCGACGTGTTTGTGAGTGGGGATCCCAAGGAG  
CAGAAGCCTCCGCAAGCTTCAGGGCTGCTCCTCCATCGCAAAGGCATCCTCAAACCTCAAT  
GGCAAGTTCTCCCAGACAGCCTTGGAGCTCGCGGGCCCCCACCACCTTCGGCTCCCTGGAT  
GAACTCGCCCCACCTCGCCCCCTGGCCCCGGGCCAGCCGACCCTCAGGGGCTGTGAGCGAG  
GACAGCATCCTGTCCTCTGAGTCCTTTGACCAGCTGGACTTGCTTGAACGGCTCCCAGAG  
CCCCCACTGCGGGGCTGTGTGTCTGTGGACAACCTCACGGGGCTTGAGGAGCCCCCTCA  
GAGGGCCCTGGAAGCTGCCTGAGGCGCTGGCGGCAGGATCCTTTGGGGGACAGCTGCTTT  
TCCCTGACAGACTGCCAGGAGGTGACAGCGACCTACCGACAGGCACTGAGGGTCTGCTCA  
AAGCTCACCTGAGTGGAGTAGGCATTGCCCCAGCCCGGTGAGGCTCTCAGATGCAGCTGG  
TTGCACCCCGAGGGGAGATGCCTTCTCCCCCACCTCCCAGGACCTGCATCCCAGCTCAGA  
AGGCTGAGAGGGTTTGCAGTGGAGCCCTGAGCAGGGCTGGATATGGGAAGTAGGCAAATG  
AAATGCGCCAAGGGTTCAGTGTCTGTCTTCAGCCCTGCTGAACGAAGAGGATACTAAAGA  
GAGGGGAACGGGAATGCCCCGCGACAGAGTCCACATTGCCTGTTTCTTGTGTACATGGAGG  
GGCCACAGAGA

SEQ ID NO: 40\_AA426580\_H, MAK\_V\_H

ATGCCGGCGGCGGGCGGGGACGGGCTCCTGGGGGAGCCGGCGGCGCCTGGGGGCGGCGGC  
GGCGCGGAGGACGCGGCCAGGCCCGCGGCGGCCTGCGAGGGAAGTTTCCTGCCTGCCTGG  
GTGAGCGGCGTGCCCCGCGAGCGGCTCCGCGACTTCCAGCACCAAGCGCGTGGGCAAC  
TACCTCATCGGCAGCAGGAAGCTGGGCGAGGGCTCCTTTGCCAAGGTGCGCGAGGGGCTG  
CACGTGCTGACCGGGGAGAAGGTGGCCATAAAAGTCATTGATAAGAAGAGAGCCAAAAAG  
GACACCTATGTCACCAAAAACCTGCGGCGAGAGGGTCAGATCCAGCAGATGATCCGCCAC  
CCCAATATCACTCAGCTCCTTGATATTTTAGAAACGGAAAAACAGCTACTACCTGGTCATG  
GAGCTGTGCCCTGGGGGCAACCTGATGCACAAGATCTATGAGAAGAAGCGGCTGGAGGAG

## FIGURE 2EE

TCCGAAGCCCCGCAGATACATCCGACAGCTCATCTCTGCCGTAGAGCACCTGCACCCGGGGCC  
GGGGTGGTCCACAGAGACTTGAAGATAGAGAATTTGCTACTAGATGAAGACAATAATATC  
AAGCTGATTGACTTTGGTTTGAGCAACTGCGCAGGGATCCTGGGTTACTCGGATCCGTTG  
AGCACACAGTGTGGCAGCCCTGCCTACGCTGCACCTGAACTGCTCGCCAGGAAGAAATAC  
GGCCCCAAAATCGATGTCTGGTCCATAGGTGTGAACATGTATGCCATGTTGACCGGGACG  
CTGCCTTTTACGGTGGAGCCTTTTACGCCTGAGGGCTTTGTACCAGAAGATGGTAGACAAA  
GAAATGAACCCCCCTCCCCACTCAGCTCTCCACAGGTGCCATCAGTTTCCTGCGCTCTCTC  
CTGGAACCGGATCCTGTGAAGAGGCCAAATATTTCAGCAGGCACTGGCGAATCGCTGGCTT  
AATGAGAATTACACGGGCAAAGTGCCCTGTAATGTCACCTATCCCAACAGGATTTCTCTG  
GAAGATCTGAGCCCGAGCGTCGTGCTGCACATGACCGAGAAGCTGGGTTACAAGAACAGC  
GACGTGATCAACACTGTGCTCTCCAACCGCGCCTGCCACATCCTGGCCATCTACTTCCTC  
TTAAACAAGAACTGGAGCGCTATTTGTGTCAGGGAAATCTGACATCCAGGACAGCCTCTGC  
TACAAGACCCGGCTCTACCAGATAGAAAAGTACAGGGCCCCCAAGGAGTCCTATGAGGCC  
TCTCTGGACACCTGGACACGAGATCTTGAATTCCATGCCGTGCAGGATAAAAAGCCCCAA  
GAACAAGAAAAAAGAGGGGATTTTCTTCATCGACCATTTCTCCAAGAAGTTGGACAAGAAC  
CTGCCCTCGCACAAACAGCCCTCAGGCTCGCTTATGACACAGATTCAGAACACCAAAGCC  
CTCCTGAAGGACCGGAAGGCCTCCAAGTCCAGCTTCCCCGACAAAGATTCCTTTGGCTGC  
CGCAATATTTTCCGCAAAACCTCAGATTCCAATTGTGTGGCTTCTTCTTCCATGGAGTTC  
ATCCCCGTGCCACCGCCCAGGACCCCGAGGATTGTGAAGAAACCGGAGCCCCATCAGCCA  
GGGCCCGGAAGCACTGGCATCCCCACAAGGAAGACCCCTGATGCTGGACATGGTGC GC  
TCCTTCGAGTCTGTGGATCGCGACGACCACGTAGAAGTGCTGTCTCCCTCTCATCACTAC  
AGGATTCTGAACTCCCCGGTCAGCTTGGCTCGCAGAAATTCCAGCGAGAGGACGCTGTCC  
CCGGGTCTGCCATCCGGAAGCATGTGCGCTCTCCATACTCCTTTGCATCCAACCTCTGGTC  
TCTTTTGCTCACGAAGATAAGAACAGCCCCCAAAAGAGGAGGGCCTGTGTTGCCACCT  
CCGGTTCCAGCAATGGCCCCATGCAGCCTCTGGGGAGCCCCAATTGTGTGAAAAGCCGA  
GGCCGGTTCCCTATGATGGGCATCGGACAGATGTTAAGGAAGCGCCATCAGAGTCTGCAG  
CCATCTGCAGATAGGCCCTGGAGGCCAGCCTGCCCCCACTGCAGCCCCTAGCCCCTGTG  
AACCTTGCCTTTGACATGGCCGATGGGGTCAAGACCCAGTGCTAA

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ATGGACACAAAGCTGAACATGCTGAACGAGAAGGTGGACCAGCTCCTGCACTTCCAAGAA  
GATGTACACAGAGAAGTTGCAGAGCATGTGCCGAGACATGGGCCACCTGGAGCGGGGCCTG  
CACAGGCTGGAGGCCTCCCGGGCACCGGGCCCCGGGCGGGGCTGATGGGGTTCCCCACATT  
GACACCCAGGCTGGGTGGCCCCGAGGTCCTGGAGCTGGTGAGGGCCATGCAGCAGGATGCC  
GCCAGCACGGTGCCAGGCTGGAGGCCCTCTTCAGGATGGTGGCTGCGGTGGACAGGGCC  
ATCGCTTTGGTGGGGGCCACGTTCCAGAAATCAAAGGTGGCGGATTTCCCTCATGCAGGGG  
CGTGTGCCCTGGAGGAGAGGCAGCCAGGTGACAGCCCTGAGGAGTGGGTAAAAGAGGAG  
GAGGTCTGTTTCATGCCTCCAGTTCCCCCAGCTCCGGGGGCAGCAGGACAGAGCCTGCAG  
AAGGATAAGGGGGAGCTGTCTGCCGAGCAGGGGATCTGGGCCACATTGATGACGCTGGTG  
ATCATGGTGACAGCGGCAAATAAAGAGCGAGTGGAAGAAGAGGGAGGAAAACCAAAGCAT  
GTGCTGAGCACCAGTGGGGTGCACTCTGATGCCAGGGAGCCTGGGGAAGAGAGCCAGAAG  
GCGGACGTGCTGGAGGGGACAGCGGAGAGGCTGCCCCCATCAGAGCGTCAGGGCTGGGA  
GCTGACCCCGCCCAGGCAGTGGTCTCACCGGGCCAGGGAGATGGTGTTCCTGGCCCAGCC  
CAGGCATTCCCTGGCCACCTGCCCCCTGCCCAAAAGGTGGAAGCCAAGGCTCCTGAGACA  
CCCAGCGAGAACCTCAGGACTGGCCTGGAATTGGCTCCAGCACCCGGCAGGGTCAATGTG  
GTCTCCCCGAGCCTGGAGGTTGCACCAGGTGCAGGACAAGGAGCATCGTCCAGCAGGCCCT  
GACCCTGAGCCCTTAGAGGAAGGCACGAGGCTGACTCCAGGGCCTGGCCCTCAGTGCCCA  
GGGCCTCCAGGGCTGCCAGCCCAGGCCAGGGCAACCCACAGTGGTGGAGAAACACCTCCA  
AGGGCAGCCCTGCTGAAGGGCGCTGTGGCCCCGGGCTTCTCTCGGAGGGACCTGGTGT  
CCTAGCATCTTCTGCGCCTGCCTAGGGATCTCCATCCACATAACAAGAGATGGATACTCCT



## FIGURE 2FF

GGGGAGATGCTGATGACAGGGCAGGGGCAGCCTTGGACCCACCCCTCACCACAGAGGGCTCCA  
GCAGCTGCCCCAGCCAGSCAAAGCAAGGGCCACCTGGGACCCGGGGCGCTGCCTCCAAGGCCCT  
GGGACTGAGCCCAGGAGAACAGACCCCTGAAGGAGCCAGAGAGCTCTCCCCGCTGCAGGAG  
AGCAGCAGCCCCGGGGGGAGTGAAGGCAGAGGAGGAGCAAAGGGCTGGGGGCCGAGCCTGGC  
ACGAGACCAAGCTTGGCCAGGAGTGACGACAATGACCACGAGGTTGGGGGCCCTGGGGCCTG  
CAGCAGGGGCAAAAGCCCCAGGGGGGGGAAACCCCTGAGCCTGAGCAGGACTGTGCAGCCAGG  
GCTCCCGGTGAGAGCTGAAGCAGTAAGGAGGATGCCCCCAGGGCGCCGAGGCTGGCAGCGTG  
GTTCTGGATGACAGTCCGGCCCCACCAGCTCCTTTTGAACACCGGGTAGTGAGCGTCAAG  
GAGACCTCCATCTCTGCGGGTTACGAGGTGTGCCAGCACGAAGTCTTGGGAGGGGGTCCG  
TTTGGCCAGGTCCACAGGTGCACAGAGAAGTCCACAGGCCTCCCCTGGCTGCCAAGATC  
ATCAAAGTGAAGAGCGCCAAGGACCGGGAGGACGTGAAGAACGAGATCAACATCATGAAC  
CAGCTCAGCCACGTGAACCTGATCCAGCTCTATGACGCCTTCGAGAGCAAGCACAGCTGC  
ACCCTTGTCATGGAGTACGTGGACGGGGGTGAGCTCTTCGACCGGATCACAGATGAGAAG  
TACCACCTGACTGAGCTGGATGTGGTCCTGTTCAACCAGGCAGATCTGTGAGGGTGTGCAT  
TACCTGCACCAGCACTACATCCTGCACCTGGACCTCAAGCCGGAGAACATATTGTGCGTC  
AATCAGACAGGACATCAAATTAAGATCATTGACTTTGGGCTGGCCAGAAGGTACAAGCCT  
CGAGAGAAGCTGAAGGTGAACCTTCGGCACTCCTGAGTTCCTGGCCCCAGAAGTCGTCAAT  
TATGAGTTTGTCTCATTCCCCACAGACATGTGGAGTGTGGGAGTCATCACCTACATGCTA  
CTCAGTGGCTTGTCCCCATTTCTAGGGGAAACAGATGCAGAGACCATGAATTTTCATTGTA  
AACTGTAGCTGGGATTTTGTATGCTGACACCTTTGAAGGGCTCTCGGAGGAGGCCAAGGAC  
TTTGTTTCCCGGTTGCTGGTCAAAGAGAAGAGCTGCAGAATGAGTGCCACACAGTGCCTG  
AAACACGAGTGGCTGAATAATTTGCCTGCCAAAGCTTCAAGATCCAAAACCTCGTCTCAAA  
TCCCAACTACTGCTGCAGAAATACATAGCTCAAAGAAAATGGAAGAAACATTTCTATGTG  
GTGACTGCTGCCAACAGGTTAAGGAAATTTCCAACCTCTCCCTAA

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GGGGAGATGGCGCTGTTTGTAGTGCCTGGTGGCGGGGGCCCACTGACGTGGAGGTGGATTGG  
CTGTGCCGTGGCCGCCTGCTGCAGCCTGCACTGCTCAAATGCAAGATGCATTTTCGATGGC  
CGCAAATGCAAGCTGCTACTTACATCTGTACATGAGGACGACAGTGGCGTCTACACCTGC  
AAGCTCAGCACGGCCAAAGATGAGCTGACCTGCAGTGCCCGGCTGACCGTGCGGCCCTCG  
TTGGCACCCCTGTTACACGGCTGCTGGAAGATGTGGAGGTGTTGGAGGGCCGAGCTGCC  
CGTTTCGACTGCAAGATCAGTGGCACCCCGCCCCCTGTTGTTACCTGGACTCATTTTGGC  
TGCCCCATGGAGGAGAGTGAGAACTTGCGGCTGCGGCAGGACGGGGGTCTGCACTCACTG  
CACATTGCCCATGTGGGCAGCGAGGACGAGGGGCTCTATGCGGTGAGTGTGTTAACACC  
CATGGCCAGGCCCCTGCTCAGCCCAGCTGTATGTAGAAGAGCCCCGGACAGCCGCCTCA  
GGCCCCAGCTCGAAGCTGGAGAAGATGCCATCCATTCCCGAGGAGCCAGAGCAGGGTGAG  
CTGGAGCGGCTGTCCATTCCCGACTTCCTGCGGCCACTGCAGGACCTGGAGGTGGGACTG  
GCCAAGGAGGCCATGCTAGAGTGCCAGGTGACCGGCCTGCCCTACCCCAACCATCAGCTGG  
TTCCACAATGGCCACCGCATCCAGAGCAGCGACCGGGCGCATGACACAGTACAGGGAT  
GTCCATCGCTTGGTGTTCCTGCCGTGGGGCCTCAGCACGCCGGTGTCTACAAGAGCGTC  
ATTGCCAACAAAGCTGGGCAAAGCTGCCTGCTATGCCACCTGTATGTCACAGATGTGGTC  
CCAGGCCCTCCAGATGGCGCCCCCGCAGGTGGTGGCTGTGACGGGGAGGATGGTCACACTC  
ACATGGAACCCCCCAGGAGTCTGGACATGGCCATCGACCCGGACTCCCTGACGTACACA  
GTGCAGCACCAGGTGCTGGGCTCGGACCAGTGGACGGCACTGGTCACAGGCCTGCGGGAG  
CCAGGGTGGGCAGCCACAGGGCTGCGTAAGGGGGTCCAGCACATCTTCCGGGTCTCTCAGC  
ACCACTGTCAAGAGCAGCAGCAAGCCCTCACCCCTTCTGAGCCTGTGCAGCTGCTGGAG  
CACGGCCCAACCCTGGAGGAGGGCCCTGCCATGCTGGACAAACCAGACATCGTGTATGTG  
GTGGAGGGACAGCCTGCCAGCGTCACCGTCACATTCAACCATGTGGAGGGCCAGGTCTGT  
TGGAGGAGCTGCCGAGGGGGCCCTCCTAGAGGCACGGGGCCGGTGTGTACGAGCTGAGCCAG  
CCAGATGATGACCAGTACTGTCTTCGGATCTGCCGGGTGAGCCGCCGGGACATGGGGGGC

## FIGURE 2GG

CTCACCTGCACCGCCCCGAAACCGTCACGGCACACAGACCTGCTCGGTACATTGGAGCTG  
GCAGAGGCCCCCTCGGTTTGAGTCCATCATGGAGGACGTGGAGGTGGGGGCTGGGGAAACT  
GCTCGCTTTGCGGTGGTGGTTCGAGGGGAAAACCACTGCCGGACATCATGTGGTACAAGGAC  
GAGGTGCTGCTGACCGAGAGCAGCCATGTGAGCTTCGTGTACGAGGAGAATGAGTGCTCC  
CTGGTGGTGGTCTCAGCACGGGGGGCCAGGATGGAGGGCTCTACACCTGCACCGCCCCAGAAC  
CTGGCGGGTGAGGTCTCCTGCAAAGCAGAGTTGGCTGTGCATTTCAGCTCAGACAGCTATG  
GAGGTTCGAGGGGGTTCGGGGAGGATGAGGACCATCGAGGAAGGAGACTCAGCGACTTTTAT  
GACATCCACCAGGAGATCGGCAGGGGTGCTTTCTCCTACTTGCGGCGCATAGTGAGGCGT  
AGCTCCGGCCTGGAGTTTGCGGCCAAGTTCATCCCCAGCCAGGCCAAGCCAAAGGCATCA  
GCGCGTCGGGAGGCCCCGGCTGCTGGCCAGGCTCCAGCACGACTGTGTCTCTACTTCCAT  
GAGGCCTTCGAGAGGCGCCGGGGACTGGTCATTGTACCCGAGCTCTGCACAGAGGAGCTG  
CTGGAGCGAATCGCCAGGAAACCCACCGTGTGTGAGTCTGAGATCCGGGGCCTATATGCGG  
CAGGTGCTAGAGGGGAATACACTACCTGCACCAGAGCCACGTGCTGCACCTCGATGTCAAG  
CCTGAGAACCTGCTGGTGTGGGATGGTGTGCGGGCGAGCAGCAGGTGCGGATCTGTGAC  
TTTGGGAATGCCCAGGAGCTGACTCCAGGAGAGCCCCAGTACTGCCAGTATGGCACACCT  
GAGTTTGTAGCACCCGAGATTGTCAATCAGAGCCCCGTGTCTGGAGTCACTGACATCTGG  
CCTGTGGGTGTTGTTGCCTTCCTCTGTCTGACAGGAATCTCCCCGTTTGTTGGGGAAAAT  
GACCGGACAACATTGATGAACATCCGAAACTACAACGTGGCCTTCGAGGAGACCACATTC  
CTGAGCCTGAGCAGGGAGGCCCCGGGGCTTCCTCATCAAAGTGTTGGTGCAGGACCGGCTG  
AGACCTACCGCAGAAGAGACCCTAGAACATCCTTGGTTCAAACTCAGGCAAAGGGCGCA  
GAGGTGAGCACGGATCACCTGAAGCTATTCTCTCCCCGGCGGAGGTGGCAGCGCTCCCAG  
ATCAGCTACAAATGCCACCTGGTGTGCGCCCCATCCCCGAGCTGCTGCGGGCCCCCCCCA  
GAGCGGGTGTGGGTGACCATGCCCAGAAGGCCACCCCCCAGTGGGGGGCTCTCATCCTCC  
TCGGATTCTGAAGAGGAAGAGCTGGAAGAGCTGCCCTCAGTGCCCCGCCCCACTGCAGCCC  
GAGTTCTCTGGCTCCCCGGGTGTCCCTCACAGACATTCCCCTGAGGATGAGGCCCTGGGG  
ACCCCAGAGACTGGGGCTGCCACCCCCATGGACTGGCAGGAGCAGGGAAGGGCTCCCTCT  
CAGGACCAGGAGGCTCCCAGCCCAGAGGGCCCTCCCCCTCCCCAGGCCAGGAGCCCCGCAGCT  
GGGGCTAGCCCCAGGCGGGGAGAGCTCCGCAGGGGCAGCTCGGCTGAGAGCGCCCTGCCC  
CGGGCCCCGGCGCGGGAGCTGGGGCCGGGGCCTGCACAAGGCGGCGTCTGTGGAGCTGCCG  
CAGCGCCGGAGCCCCGGCCCCGGGAGCCACCCGCTGGCCCCGGGGAGGCCTGGGTGAGGGC  
GAGTATGCCCAGAGGCTGCAGGCCCTGCGCCAGCGGCTGCTGCGGGGAGGCCCCGAGGAT  
GGCAAGGTCAGCGGCCTCAGGGGTCCCCTGCTGGAGAGCCTGGGGGGCCGTGCTCGGGAC  
CCCCGGATGGCACGAGCTGCCTCCAGCGAGGCAGCGCCCCACCACCAGCCCCCACTCGAG  
AACCAGGGGCTGCAAAAGAGCAGCAGCTTCTCCCAGGGTGAGGCGGAGCCCCGGGGCCGG  
CACCGCCGAGCGGGGGCGCCCCCTCGAGATCCCCGTGGCCAGGCTTGGGGCCCCGTAGGCTA  
CAGGAGTCTCCTTCCCTGTCTGCCCTCAGCGAGGCCCAGCCATCCAGCCCTGCACGGCCC  
AGCGCCCCCAAACCCAGTACCCCTAAGTCTGCAGAACCTTCTGCCACCACACCTAGTGAT  
GCTCCGCAGCCCCCGCACCCCAGCCTGCCCAAGACAAGGCTCCAGAGCCCAGGCCAGAA  
CCAGTCCGAGCCTCCAAGCCTGCACCACCCCCCAGGCCCTGCAAACCTAGCGCTGCCC  
CTCACACCCTATGCTCAGATCATTCAGTCCCTCCAGCTGTCAGGCCACGCCCAGGGCCCC  
TCGCAGGGCCCTGCCGCGCCGCTTCAGAGCCCAAGCCCCACGCTGCTGTCTTTGCCAGG  
GTGGCCTCCCCACCTCCGGGAGCCCCCGAGAAGCGCGTGGCCTCAGCCGGGGGTCCCCCG  
GTGCTAGCCGAGAAAGCCCGAGTTCCACCGGTGCCCCCAGGCCAGGCAGCAGTCTCAGT  
AGCAGCATCGAAAACCTTGAGTCGGAGGCCGTGTTTCGAGGCCAAGTTCAAGCGCAGCCGC  
GAGTCGCCCCCTGTGCTGGGGCTGCGGCTGCTGAGCCGTTCGCGCTCGGAGGAGCGCGGC  
CCCTTCCGTGGGGCCGAGGAGGAGGATGGCATATACCGGCCAGCCCCGGCGGGGACCCCC  
CTGGAGCTGGTGCACGGCCTGAGCGCTCACGCTCGGTGCAGGACCTCAGGGCTGTGGA  
GAGCCTGGCCTCGTCCGCGCCTCTCGCTGTCACTGTCCCAGCGGCTGCGGCGGACCCCT  
CCCGCGCAGCGCCACCCGGCCTGGGAGGCCCGCGGGCGGGGACGGAGAGAGCTCGGAGGGC  
GGGAGCTCGGCGCGGGGCTCCCCGGTGCTGGCGATGCGCAGGCGGCTGAGCTTCACCCTG

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## FIGURE 2HH

GAGCGGCTGTCCAGCCGATTGCAGCGCAGTGGCAGCAGCGAGGACTCGGGGGGGCGCGTCC  
GGCCGCAGCAGCGCCGCTGTTCGGACGGCTTCGCAGGGCCACGTCCGAGGGCGAGAGTCTG  
CGGCGGCTTGGGCTTCGGCACAACCAAGTTGGGCGGCGCAGGCCCGGCCACCAGGCTTCC  
GCGGAGTCCCTGGGCTCCGAGGGCCAGCGCCACGTGGGGCTCCTCAGCCCCAGGGGAAAGC  
CGAAGCCGGCTCCGCTGGGGCTTCTCTCGGCCGCGGAAGGACAAGGGGTTATCGCCACCA  
AACCTCTCTGCCAGCGTCCAGGAGGAGTTGGGTACCCAGTACGTGCGCAGTGAGTCAGAC  
TCCCCCCCAGTCTTCCACATCAAACCTCAAGGACCAGGTGCTGCTGGAGGGGGAGGCAGCC  
ACCCTGCTCTGCCTGCCAGCGGCCTGCCCTGCACCGCACATCTCCTGGATGAAAGACAAG  
AAGTCCTTGAGGTCAGAGCCCTCAGTGATCATCGTGTCCTGCAAAGATGGGCGGCAGCTG  
CTCAGCATCCCCCGGGCGGGCAAGCGGCACGCCGGTCTCTATGAGTGCTCGGCCACCAAC  
GTACTGGGCAGCATCACCAGCTCCTGTACCGTGGCTGTGGCCCCGAGTCCCAGGAAAGCTA  
GCTCCTCCAGAGGTAACCCAGACCTACCAGGACACGGCGCTGGTGCTGTGGAAGCCGGGA  
GACAGCCGGGCACCTTGACGTATACGCTGGAGCGGCGAGTGGAATGGGGAGTCTGTGTGG  
CACCTGTGAGCTCAGGCATCCCCGACTGTTACTACAACGTGACCCACCTGCCAGTTGGC  
GTGACTGTGAGGTTCCGTGTGGCCTGTGCCAACCGTGCTGGGCAGGGGGCCCTTCAGCAAC  
TCTTCTGAGAAGGTCTTTGTGTCAGGGGTACTCAAGATTCTTCAGCTGTGCCATCTGCTGCC  
CACCAAGAGGGCCCCCTGTACCTCAAGGCCAGCCAGGGCCCCGGCCTCCTGACTCTCCTACC  
TCACTGGCCCCACCCCTAGCTCCTGCTGCCCCCACACCCCCGTGAGTCACTGTCAGCCCC  
TCATCTCCCCCCCACACCTCCTAGCCAGGCCTTGTCCTCGCTCAAGGCTGTGGGTCCACCA  
CCCCAAACCCCTCCACGAAGACACAGGGGCCTGCAGGCTGCCCCGGCCAGCGGAGCCCCACC  
CTACCCAGTACCCACGTACCCCCAAGTGAGCCCAAGCCTTTCGTCTCTTGACACTGGGACC  
CCGATCCCAGCCTCCACTCCTCAAGGGGTAAACCAGTGTCTTCTCTACTCCTGTGTAT  
GTGGTGACTTCCTTTGTGTCTGCACCACCAGCCCCCTGAGCCCCCAGCCCCCTGAGCCCCCT  
CCTGAGCCTACCAAGGTGACTGTGCAGAGCCTCAGCCCCGGCCAAGGAGGTGGTCAGCTCC  
CCTGGGAGCAGTCCCCGAAGCTCTCCCAGGCCTGAGGGTACCACTCTTCGACAGGGTCCC  
CCTCAGAAACCCCTACACCTTCTGAGGAGAAAGCCAGGGGGCCGCTTTGGTGTTGTGCGA  
GCGTGCCGGGAGAAATGCCACGGGGCGAACGTTTCGTGGCCAAGATCGTGCCCTATGCTGCC  
GAGGGCAAGCCGCGGGTCTGCAGGAGTACGAGGTGCTGCGGACCCTGCACCACGAGCGG  
ATCATGTCCCTGCACGAGGCCTACATCACCCCTCGGTACCTCGTGCTCATTGCTGAGAGC  
TGTGGCAACCGGGAACCTCCTCTGTGGGCTCAGTGACAGGTTCCGGTATTCTGAGGATGAC  
GTGGCCACTTACATGGTGCAGCTGCTACAAGGCCTGGACTACCTCCACGGCCACCACGTG  
CTCCACCTAGACATCAAGCCAGACAACCTGCTGCTGGCCCCCTGACAATGCCCTCAAGATT  
GTGGACTTTGGCAGTGCCCCAGCCCTACAACCCCCAGGCCCTTAGGCCCTTGGCCACCGC  
ACGGGCACGCTGGAGTTCATGGCTCCGGAGATGGTGAAGGGAGAAACCATCGGCTCTGCC  
ACGGACATCTGGGGAGCGGGTGTGCTCACTTACATTATGCTCAGTGAGCGCTCCCCGTTC  
TATGAGCCAGACCCCCAGGAAACGGAGGCTCGGATTGTGGGGGGCCGCTTTGATGCCTTC  
CAGCTGTACCCCAATACATCCCAGAGCGCCACCCTCTTCTTGCGAAAGGTTCTCTCTGTA  
CATCCCTGGAGCCGGCCCTCCCTGCAGGACTGCCTGGCCCCACCCATGGTTGCAGGACGCC  
TACCTGATGAAGCTGCGCCGCCAGACGCTCACCTTCACCACCAACCGGCTCAAGGAGTTC  
CTGGGCGAGCAGCGGCGGCGCCGGGCTGAGGCTGCCACCCGCCACAAGGTGCTGCTGCGC  
TCCTACCCTGGCGGCCCCCTAGAGGCACGGACCACAGCCAGGCCTCGGGCTTCAACTGGGG  
TTCCCAACCAATGCCACGGGACATTCCAGGGGCCACGCTGAGCCAGGCGGGCCTGGGGCTT  
CGGTTACCACCAGCAGCAACATCTGGCTGGGCTCTTACCTCATAGACCTTCAAGGACAGA  
GACCCAGGGCCTGGACCTGATGCCACCCAGGCCAAAGCCAGAGTGGGAGACCCATTGG  
TCAGGCTCAGCAGGGTGGGAACAGGCAGAGGGACAAGAGGGGAATGGAGAAGTGGAGAGG  
AAAAGGAATCGAGGGACAGGAAGGGGGAGGCTCTAGGAAGGTTCTGGGTTGGGGGTCAGT  
GCATCTCAGGGAGAACCAAGGAAGGTGGGCATGGCTGGAGAGGAGGAAAAGGAAGGAGCC  
CCAGGTGTCAGGGCAGTAGGCTGGGAGTCAGTGTGGCAAAGCGGGGGCAGGACACAGATA  
CAGTGGCAGGGGGCCAGGGCTGGGACATGAGAGAAGGCAGCGAGGCGGCAGAGGGAGAAG  
AGAGGACTCAGGTGGAGGTGGGGTGGGTGAGCTGTCAGCATCCCTCAGAGGAGAAATGTG



## FIGURE 2II

GAGAGCTGGAGGCCAGCAGTCACTCACACTCGCTCTGTCCTCCTGTCCAGTGGATACAGC  
CCTGGGCGCTCTGCTGGCCCAAGGATGTCCCCACTGCCCTCCATGGCCTTTGGCCTTCT  
TCCCATTCATATTTATTTATTTATTGACTTTTATGAAGTTTCCCCTTCCATCCGATCCCT  
ACTGCCCATGTTGTCTGACCATCCCTCCCAGCCATCCAGCTGTCTGTCTGTCTGCCACA  
AGGAAATAAAAATGGCAAGCAGCAAAAAA

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GCCACGGACATCTGGGGAGCGGGTGTGCTCACCTACATCATGCTTAGTGGGTACTCCCCA  
TTCTATGAGCCAGACCCCCAGGAAACAGAGGCTCGGATTGTTGGGGGTGCTTTTGATGCC  
TTCCAGTTGTATCCTAACACATCCCAGAGTGCCACCCTCTTCTTGAGAAAGGTCCTCTCA  
GTACATCCCTGGAGCCGGCCCTCTCTGCAGGACTGCTTGGCCCCACCCATGGCTGCAAGAT  
GCCTACCTGATGAAGCTGCGCCGCCAGACACTCACCTTCACCACCAACCGGCTCAAGGAA  
TTCCTGGGCGAGCAGCGGCGACGTGCGGCTGAGGCTGCTACCCGTCACAAGGTGCTGCTC  
CGCTCCTACCCTGGCAGCCCCCTAGGTGGCACAGACCGCAGCCCCGGCCACGGGCTTCAACT  
TGGGTTCTCACTCGCGCTGCCAAGGGACATTCCAGAGCCCATGCTGAGCTGGACAGGCAG  
GGGCTTCAGATACCAGCAGCAGCAGCAGCAGCAGCAGCAACATCTGGCTGGGCTATT  
ACCTCATGGACCTAAGAGGACAAGGCCCTGGGGCTTCAGCCGAATGTCACCCCGGCCATA  
ACCAGAGCAGGAGACCCACTGGCCAGGCTGGGCAAGGGTGAGAGCAGAAAGAGGCAAAGA  
GGGAGTTGGGAAGTGAAGAATGAGACGGAGGATAGAGAGGGAGGAGTTTGAGGAAGGTTT  
TAGGCTGGAGTGGAATGCTATATCTCAGGGAGAAGCCAGAAGGGGACATGGCTGAAGAGG  
AAGAAGGACCCTGTGATGTGGGAATGTGGTGGAGAGGAGGACTGGACATAGAGAGTGTGC  
CAGGAGCCAGAGCAGAGACATAAGGGAGGGCAGAAGGGTAGAAGGCAACAGGAGTGGGCT  
CAGGGGTGGCAGGGCAGGCCAGCAGCTGCATCTTCAGAAAGAGAGAGGAGAAAGGCAAAG  
AGACGAAAGGCCGCTCCAGCTGGTCTCCTGTCCCAGCCGATGCAGTTCTGGGCGTTCTCC  
ACTGGCCCAGGGATGTCCTCACTGCTCCTCCATGGCCTTTGCCCTCCTTCCCATTGTAT  
TTATTTATTTATTGCCTTTTGTGGAGTTTCCTTTCTATCCAGTCCCTAGTGCCTATGTTG  
TCCCGACCATCCCCCTTCAGTCACCCAGCTGTCTGTGCAGCTGTCTGTCTGTCTGTCTGTCACA  
AGGAAAATAAAAACAAAACAAAACAAAACAAAACAAAACAAAACAAAACAAAACAGC

SEQ ID NO: 44\_R19772\_H

ATGAAGGGCGGCGACAGGGCTTACACCCGAGGTCCCTCTTTGGGGTGGCTCTTTGCTAAG  
TGCTGCTGTTGCTTCCCGTGTAGAGATGCATACTCTCATTCCCTCAAGCGAGAATGGAGGC  
AAGTCCGAGTCCGTAGCCAACCTGCAGGCCAGCCCTCCCTGAACCTTCATCCACAGTTCC  
CCGGGTCCCAAGCGCTCCACCAACACTCTTAAGAAGTGGCTGACGAGTCCTGTGCGTCGG  
CTCAACAGCGGGAAGGCAGATGGAAACATCAAAAAGCAGAAGAAAGTTGCGGATGGTCCG  
AAGAGCTTTGACCTGGGATCTCCCAAGCCTGGGGATGAAACAACCCCTCAGGGAGACAGC  
GCTGATGAGAGCAAGAAAGGTTGGGGTGAAGATGAGCCGGATGAAGAGTCACACACACCC  
CTCCCACCACCTATGAAGATTTTGTGACAACGACCCTACACAGGATGAAATGTCCTCCTCT  
TTGCTAGCAGCCCCGGCAGGCTTCCACTGAAGTACCTACTGCTGCAGACCTTGTCAATGCA  
ATAGAAAAGTTGGTCAAAAACAAGCTGAGTCTAGAAGGAAGCTCATACCGGGGGAGCTTG  
AAAGACCCTGCAGGCTGCCTGAATGAGGGGATGGCCCCACCCACACCTCCTAAAAATCCA  
GAAGAAGAACAGAAAGCCAAGGCCCTGAGAGGCAGGATGTTTGTCTGAATGAGCTGGTA  
CAGACAGAGAAAGACTATGTCAAGGATCTGGGCATTGTGGTGGAGGGCTTCATGAAGAGA  
ATAGAAGAAAAGGGTGTCCCTGAGGATATGCGAGGAAAGGACAAAATCGTGTTTGGAAAT  
ATTCATCAGATTTATGACTGGCATAAGGATTTTTTTCCTGGCGGAACTGGAAAAGTGTATC  
CAGGAGCAAGACAGATTGGCACAGCTCTTTATTAAGCACGAGCGGAAGCTGCACATCTAC  
GTGTGGTATTGTCAGAATAAGCCGCGCTCAGAGTACATCGTTGCTGAGTATGACGCCTAC  
TTTGAGGAGGTAACACAGGAGATAAATCAGAGGCTGACACTGAGTGACTTCCTCATCAAG  
CCCATTTCAGAGAATAACAAAATACCAGTTGCTCCTCAAGGACTTCCTGAGATACAGTGAG  
AAGGCTGGTTTGGAGTGTTTCAAGATATCGAGAAAGCAGTGGAGTTAATGTGCCTTGTTCCC

## FIGURE 2JJ

AAACGCTGCAATGACATGATGAATCTAGGACGTCTGCAGGGCTTTGAGGGGCACTCTGACT  
GCTCAGGGGGAAGCTACTGCAGCAGGACACATTCTATGTGATCGAGCTGGATGCAGGGCATG  
CAGTCCCGGACCAAAGAGAGGGCGCGTGTTCCTCTTCGAGCAGATTGTCATCTTCAGTGAA  
CTGCTCAGGAAGGGATCCCTCACCCCTGGCTACATGTTCAAAAGGAGCATCAAGATGAAT  
TACTTGGTCCTGGAGGAGAATGTGGACAATGATCCCTGCAAGTTTGCACCTCATGAACAGA  
GAGACTTCTGAGAGGGTTGTTCTGCAAGCCGCCAACGCTGACATCCAGCAGGCCTGGGTG  
CAGGACATCAATCAAGTCTTAGAAACACAGCGAGACTTTTTGAATGCACTGCAATCGCCC  
ATTGAGTATCAACGGAAAGAAAGGAGCACAGCTGTGATGAGGTCTCAACCTGCCAGGCTT  
CCCCAAGCCAGCCCCAGGCCCTACTCCTCTGTTCTGCGGGCTCAGAGAAGCCCCCAAAG  
GGCTCCAGCTATAACCCACCTCTGCCTCCCCTGAAGATATCTACCTCCAATGGCAGTCCA  
GGGTTTGAATACCACCAGCCTGGGGACAAGTTCGAAGCCAGCAAGAACGACCTGGGAGGC  
TGCAATGGGACCTCGTCCATGGCCGTGATCAAAGATTACTATGCACTGAAGGAGAATGAA  
ATCTGTGTGAGCCAAGGTGAGGTGGTCCAGGTCCTCGCCGTCAACCAGCAGAACATGTGT  
CTGGTGTACCAGCCTGCCAGCGACCATTCCCCCGCCGCCGAGGGCTGGGTCCCAGGCAGC  
ATCCTGGCGCCCCCTACCAAAGCCACAGCAGCAGAAAGTAGTGACGGGAGCATCAAGAAG  
TCATGTTTCATGGCATACTCTACGCATGAGAAAGCGGGCGGAAGTGGAGAACACGGGTAAA  
AATGAAGCCACAGGGCCTCGTAAACCCAAGGATATTCTGGGCAACAAAGTCTCTGTAAA  
GAGACGAACAGTTCGAGGAATCAGAGTGTGATGATCTTGACCCTAATACTAGCATGGAG  
ATCTTAAATCCAAATTTTCATCCAAGAAGTGGCCCCAGAATTCTTGTGCCCTTGGTGGAT  
GTGACCTGCTTGCTTGGGGACACAGTGATACTGCAGTGCAAAGTCTGTGGGCGGCCAAAG  
CCCACCATCACTTGGAAGGGTCCAGACCAGAACATCCTTGACACTGATAACAGCTCAGCC  
ACATACACGGTCTCCTCTTGTGATTCTGGAGAAATCACCTGAAGATCTGTAATCTGATG  
CCCCAAGACAGTGGGATTTATACCTGCATAGCAACAAATGACCACGGGACCACATCAACG  
TCTGCAACAGTCAAAGTGCAAGGTGTTCCAGCAGCCCCCTAACCGCCCCATTGCCCAGGAG  
AGAAGCTGCACCTCCGTGATTCTCCGCTGGCTGCCCCCTCCAGCACAGGAAACTGCACT  
ATTTCTGGTTACACTGTGGAGTACAGAGAGGAAGGTCTCAGATCTGGCAGCAGTCAGTG  
GCTTCGACCTTGGACACTTACCTCGTCATCGAAGACCTTAGTCCCGGGTGTCTTATCAG  
TTCAGAGTCAGTGCCAGTAACCCCTGGGGAATCAGCCTTCCCAGCGAGCCCTCGGAGTTT  
GTGCGACTTCCAGAATACGATGCTGCTGCTGATGGTGCCACCATTTCTTGGAAGGAAAAT  
TTTGACTCAGCTTACACTGAGCTGAATGAAATTGGAAGAGGCCGTTTCTCTATAGTAAAG  
AAATGCATTCACAAAGCTACCCGCAAAGATGTGGCTGTGAAATTTGTTAACAAAAAATG  
AAGAAGAAAGAACAGGCTGCCCCAGAGGCTGCCCTGCTTCAGCACCTACAGCACCCCCAG  
TACATCACTCTCCATGACACCTATGAGTCCCCCACATCCTACATCCTGATCTTGGAAGT  
ATGGATGATGGCCGGCTCTTAGACTACCTTATGAATCATGATGAACTGATGGAGGAAAAA  
GTAGCTTTCTATATCCGAGACATCATGGAGGCTCTGCAGTACCTTCACAACTGCAGGGTT  
GCACATTTGGACATAAAGCCTGAAAACCTGCTCATTGACCTACGGATTCCAGTGCCTCGA  
GTGAAGCTCATTGACTTGGAGGATGCTGTCCAGATCTCGGGTCACTTCCACATTCACCAC  
CTGCTGGGGAACCCTGAGTTTGCTGCCCCAGAAGTCATTCAAGGCATCCCCGTCTCCCTG  
GGGACAGACATCTGGAGCATCGGGGTTCTGACATATGTCATGCTGAGTGGGGTCTCCCC  
TTCTTGATGAGAGCAAAGAGGAGACATGTATCAACGTATGCAGGGTGGATTTTCAGCTTC  
CCCCATGAATACTTCTGTGGTGTGAGCAATGCTGCCAGAGATTCATCAATGTGATCTTA  
CAGGAAGATTTTCGGAGGCGGCCACAGCAGCCACATGCTTGCAGCATCCATGGCTGCAG  
CCCCATAATGGCAGCTACTCTAAGATCCCCCTGGACACCTCCCGCCTAGCATGCTTCATA  
GAACGTGCAAGCACCAAGAAATGATGTGCGGCCTATCCCCAATGTCAAGAGCTACATTGTC  
AACCGGGTGAACCAAGGGACGTAG

SEQ ID NO: 45\_5R72\_8\_2\_H

CGCCGCTGTTTGTCTCGCGCGGCCCGTCCACTGCCCTGCGGTTGCTCTGCGGGCTGAA  
AAGTTTCTCCCGGTGCAGAATTCCGGGGCTCAGCGACAGCCTGCGCCGAGTGTGCGCACCT  
GTCGGAGACCCGCCAGTCCGCCGGCCCCGGCTTTGTTCTGTGCGGAAGTGTAGTGGTGAGA



## FIGURE 2KK

AAAACCTCCATGTCTGGGCACGCCTGGCTGATCTTCACCTCTTTCTTCTAGGACCTTCCTC  
TGGGCTGTCACGTGTGAATATGTGTCTAGTGCATCCTTAACCTGAGGACTTCACCACTTC  
GAAATTACAGTTTTTCACCATCAACTACCTTATCCTTTTTTGGCCTGGTTTTCTTCCTCAA  
CAGTGGAACATTTTTTAAAGTTGCTTTTGTGTCAGAGTTAAACAAATGGCTGATAGTGGC  
TTAGATAAAAAATCCACAAAATGCCCCGACTGTTTCATCTGCTTCTCAGAAAGATGTACTT  
TGTGTATGTTCCAGCAAAACAAGGGTTCCTCCAGTTTTTGGTGGTGGAAATGTCACAGACA  
TCAAGCATTGGTAGTGCAGAATCTTTAATTTCACTGGAGAGAAAAAAGAAAAAATATC  
AACAGAGATATAACCTCCAGGAAAGATTTGCCCTCAAGAACCTCAAATGTAGAGAGAAAA  
GCATCTCAGCAACAATGGGGTTCGGGGCAACTTTACAGAAGGAAAAGTTCCTCACATAAGG  
ATTGAGAATGGAGCTGCTATTGAGGAAATCTATACCTTTGGAAGAATATTGGGAAAAGGG  
AGCTTTGGAATAGTCATTGAAGCGACAGACAAGGAAACAGAAACGAAGTGGGCAATTAAA  
AAAGTGAACAAAGAAAAGGCTGGAAGCTCTGCTGTGAAGTTACTTGAACGAGAGGTTGAAC  
ATTCTGAAAAGTGTAACACATGAACACATCATACTGGAACAAGTATTTGAAACGCCA  
AAGAAAATGTACCTTGTGATGGAGCTTTGTGAGGATGGAGAACTCAAAGAAATTCTGGAT  
AGGAAAGGGCATTCTCAGAGAATGAGACAAGGTGGATCATTCAAAGTCTCGCATCAGCT  
ATAGCATATCTTCACAATAATGATATTGTACATAGAGATCTGAAACTGGAAAATATAATG  
GTTAAAAGCAGTCTTATTGATGATAACAATGAAATAAACTTAAACATAAAGGTGACTGAT  
TTTGGCTTAGCGGTGAAGAAGCAAAGTAGGAGTGAAGCCATGCTGCAGGCCACATGTGGG  
ACTCCTATCTATATGGCCCCCTGAAGTTATCAGTGCCACGACTATAGCCAGCAGTGTGAC  
ATTTGGAGCATAGGAGTCGTAATGTACATGTTATTACGTGGAGAACCACCCTTTTTTGGCA  
AGCTCAGAAGCGAAGCTTTTTTGAGTTAATAAGAAAAGGAGAAGTACATTTTGAAAATGCA  
GTCTGGAATTCCATAAGTGAAGTGTGCTAAAAGTGTTTTGAAACAACCTTATGAAAGTAGAT  
CCTGCTCACAGAATCACAGCTAAGGAACTACTAGATAACCAGTGGTTAACAGGCAATAAA  
CTTTCTTCGGTGAGACCAACCAATGTATTAGAGATGATGAAGGAATGGAAAAATAACCCA  
GAAAGTGTTGAGGAAAACACAACAGAAGAGAAGAATAAGCCGTCCACTGAAGAAAAGTTG  
AAAAGTTACCAACCCTGGGGAAATGTCCCTGAGACCAATTACACTTCAGATGAAGAGGAG  
GAAAAACAGTCTACTGCTTATGAAAAGCAATTTCTGCAACCAGTAAGGACAACCTTTGAT  
ATGTGCAGTTCAAGTTTCACATCTAGCAAACCTCCTTCCAGCTGAAATCAAGGGAGAAATG  
GAGAAAACCCCTGTGACTCCAAGCCAAGGAACAGCAACCAAGTACCCTGCTAAATCCGGC  
GCCCTGTCCAGAACCAAAAAGAACTCTAAGGTTCCCTCCAGTGTTGGACAGTACAAAA  
CAAAGCTGCTCTTGTTAGCACTTTGATGAGGGGGTAGGAGGGGAAGAAGACAGCCCTATG  
CTGAGCTTGTAGCCTTTTAGCTCCACAGAGCCCCGCCATGTGTTTGCACCAGCTTAAAAT  
TGAAGCTGCTTATCTCAAAGCAGCATAAGCTGCACATGGCATTAAAGGACAGCCACCAG  
TAGGCTTGGCAGTGGGCTGCAGTGGAAATCAACTCAAGATGTACACGAAGGTTTTTTAGG  
GGGGCAGATACCTTCAATTTAAGGCTGTGGGCACACTTGCTCATTTTTTACTTCAAATTCT  
TATGTTTAGGCACAGCTATTTATAGGGGAAAACAAGAGGCCAAATATAGTAATGGAGGTG  
CCAAATAATTATGTGCACTTTGCACTAGAAGACTTTGTTAGAAAATTACTAATAAACTTG  
CCATACGTATTACAGCAGAAGTGCTTCAGTCATTACATGTGTTTCGTGAGATTTTAGGTT  
GCTATAGATTGTTTAAGACAGCTTATTTTAAATGTAGAAAAATAGGAGATTTTGTAAGT  
CTTGCCATTAACTTGCTGCTAAATTCCCAATGTATTGATTAAATCAATAAAAAACAGATG  
TACTC

SEQ ID NO: 46\_SGK309\_H

GGGTCCGCAGCCCGCCCTCACAGGCCCTCCTCACTCCCCTAGGTAGATGGCCCCCTCAGG  
GCAGGCCCGGCGGACACCCCTCCCTCTGGCTGGCGGATGCAGTGCCTAGCGGCCCGCCCTT  
AAGGACGAAACCAACATGAGTGGGGGAGGGGAGCAGGCCGACATCCTGCCGGCCAACTAC  
GTGGTCAAGGATCGCTGGAAGGTGCTGAAAAAGATCGGGGGCGGGGGCTTTGGTGAGATC  
TACGAGGCCATGGACCTGCTGACCAGGGAGAATGTGGCCCTCAAGGTGGAGTCAGCCAG  
CAGCCCAAGCAGGTCTCAAGATGGAGGTGGCCGTGCTCAAGAAGTTGCAAGGTTCCGGGC  
CTCGGGCAGGGGGATGGGAAGGAAGAGATGATGAAGCCAGGGGCTAAGAGAGGGAAGGAC

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## FIGURE 2LL

CATGTGTGCAGGTTTCATTGGCTGTGGCAGGAACGAGAAGTTTAACTATGTAGTGATGCAG  
CTCCAGGGCCGGGAACCTGGCCGACCTSCGCGGTAGCCAGCCGCGAGGGCACCTTCACGCTG  
AGCACACATTGCGGCTGGGCAAGCAGATCTTGGAGTCCATCGAGGCCATCCACTCTGTG  
GGTTCTCTGCACCGTGACATCAAGCCTTCAAACCTTTGCCATGGGCAGGCTGCCCTCCACC  
TACAGGAAGTGCTATATGCTGGACTTCGGGCTGGCCCCGGCAGTACACCAACACCACGGGG  
GATGTGCGGGCCCCCTCGGAATGTGGCCGGGTTTCGAGGAACGGTTCGCTATGCCTCAGTC  
AATGCCCCACAAGAACCAGGAGATGGGGCCGCCACGACGACCTGTGGTCCCTCTTCTACATG  
CTGGTGGAGTTTGCAGTGGGCCAGCTGCCCTGGAGGAAGATCAAGGACAAGGAACAGGTA  
GGGATGATCAAGGAGAAGTATGAGCACCGGATGCTGCTGAAGCACATGCCGTCAGAGTTC  
CACCTCTTCCTGGACCACATTGCCAGCCTCGACTACTTCACCAAGCCCCGACTACCAGTTG  
ATCATGTGAGTGTGTTGAGAACAGCATGAAGGAGAGGGGCATTGCCGAGAATGAGGCCTTT  
GACTGGGAGAAGGCAGGCACCGATGCCCTCCTGTCCACGAGCACCTCTACCCCCGCCCCCA  
GCAGAACACCCGGCAGACGGCAGCCATGTTTGGGGTGGTCAATGTGACGCCAGTGCTGG  
GGACCTGCTCCGGGAGAACACCGCGGATGTGCTACAGGGAGAGCACCTGAGTGACCAGGA  
GAATGCACCCCCAATTCTGCCCGGGAGGCCCTCTGAGGGGCTGGGCCACAGTCCCCACCT  
TGTCCCCCACCCCGGGGGTCTGAGGCTGAAGTCTGGGAGGAGACAGATGTCAACCGGAA  
CAAACCTCCGGATCAACATCGGCAAAGTAACTGCCGCCAGGGCGAAGGGCGTGGGTGGCCT  
TTTCTCTACCCCCGATTCCCAGCCTTGTGCCCTGCCCTGTTCTCTAAGCACCTGT  
CCCCGCCAATCTCCCTGCTTGCCCGGCCTCTGTTTCCGGTCCCCCTCCCCGGCACTAGCC  
TCGCTGTGTCTTCCATCATCATCATCTCTGTCTCCTTCACACTGAGGAGACCATCCGCC

SEQ ID NO: 47\_AA234451\_H

GGCGCGCCAGATATCACACGTGCCAAGGGGCTGGCTCAGCGGCGGCGGGCGGCAGGAGGGG  
GAGCAGGTGCTGGCACAAGAGCAGCGGCTTGGGGGAGCCGGCAGCAGCAGTAACAGCAGC  
AGCAGCCGCGCCGCGCCGCGCCAGTAAACGCGGACCGTACCCCAGGGGACTACCCAGCCG  
GCCGGCCCTGGAAGCCGCGCTCGGGTCCCCGCCGAGTCGGCGGTGGGGGATGGGCAGGCA  
GTGGCGGTCCCGCCTGCCGAGGGTTAAACCCCGCCGGTCCCGGTCTTGAGCTGGACCAGA  
GCCCTCCTCCAGAAACCCCTGCGTCCGCCACGGCCCAGGTTAAATGGAAACCACCCTTG  
GAACTGGATGCCTGTGTAGCTGTTCTACCATATCAGTGTATTGCAATGAGTGGGGGAGGA  
GAGCAGCTGGATATCCTGAGTGTTGGAATCCTAGTGAAAGAAAGATGGAAAGTGTGAGA  
AAGATTGGGGGTGGGGGCTTTGGAGAAATTTACGATGCCTTGGACATGCTCACCAGGGAA  
AATGTTGCACTGAAGGTGGAATCAGCTCAACAACCAAAAACAAGTTCTGAAAATGGAAGTT  
GCTGTTTTGAAAAAGCTGCAAGGGAAAGACCATGTTTGTAGATTTATTGGCTGTGGGAGG  
AATGATCGATTCAACTATGTGGTCATGCAGTTGCAGGGTCGGAATCTGGCAGATCTTCGC  
CGTAGCCAGTCCCGAGGCACATTCACCATTAGTACCCTCTCCGGCTGGGTAGACAGATT  
TTGGAGTCTATTGAAAGCATTCACTCTGTGGGATCTTGNCATCGAGACATCAAACCGTCG  
AACTTCGCTATGGGTGCTTTCTTAGTACATGTAGGAAATGTTACATGCTTTGATTTTGGC  
TTGGCTCGACAATTTACCAATTCCTGTGGTGACGTCAGACCACCTCGAGCTGTGGCAGGT  
TTTCGAGGGACAGTTCGTTATGCATCAATCAACGCACATCGGAACAGGGAAATGGGAAGA  
CATGATGACCTTTGGTCCTTATTCTACATGTTGGTGGAGTTTGTGGTTGGTCAGCTGCCC  
TGGAGAAAAATAAAGGACAAGGAGCAAGTAGGCTCTATTAAGGAGAGATATGACCACAGG  
CTCATGTTGAAACATCTCCCTCCAGAATTCAGCATCTTTCTAGACCATATCTCTTCTTTG  
GATTATTTTACAAAACCAGACTACCAGCTTCTTACATCCGTGTTTGACAATAGCATCAAG  
ACTTTTGGAGTAATTGAGAGTGACCCTTTTGACTGGGAGAAGACTGGAAATGATGGCTCC  
CTAACAACCACCACTACTTCTACCACCCCTCAGTTGCACACTCGCTTGACCCCTGCTGCA  
ATTGGAATTGCCAATGCTACTCCCATCCCTGGAGACTTGCTTCGAGAAAATACAGATGAG  
GTATTTCCAGATGAACAGCTTAGCGATGGAGAAAATGGCATCCCTGTTGGTGTGTACCA  
GATAAATTGCCTGGATCTCTGGGACACCCCCGTCCCCAGGAGAAGGATGTTTGGGAAGAG  
ATGGATGCCAACAAAAACAAGATAAAGCTTGGAATTTGTAAGGCTGCTACTGAAGAGGAG  
AACAGCCATGGCCAGGCAAATGGTCTTCTCAATGCTCCAAGCCTTGGGTACCAATTCGT

## FIGURE 2MM

GTCCGCTCAGAGATTACTCAGCCAGACAGAGATATTCCTACTGGTGCGAAAGTTACGTTCC  
ATTCACAGCTTTGAGCTGGAAAAACGTCTGACCCTGGAGCCAAAGCCAGACACTGACAAG  
TTCCTTGAGACCTGGTATAAAAATAGTGTATTTTTCTTTTTTAAAGCTTCTAAGGTACCATT  
ATTATTGTTGTCATTGTTGTTATTATTATTGTATATTTCTGTGTACATAAAGTCTTTCAAA  
TAAGAAATCCTTGCAATTTTTGTAACACTGAGTCTATTCAGCTCCAATTTTCATCCATGTT  
TTTAATTATTATTATCCTGATTCTTAATTATTATAAATTCTATAGCATATCCTTTGGCTT  
TGGAAGCTGAGCAGTAAGAGCTGATGACTTCCTAACACTAGGTACAAGTTAAATGAACAT  
TTTTACAGTAACTTTGTTTAGAAAGTAATCTCTTCCACACAACAGTGTAAGTGCTGGAGAG  
GGCATGATAAAGATGGCATTAGGCAGAGATGAGGGGAATACATAAAGGAGGGGAAAAAGT  
AATTCATACACAAGGGACGGTGAGTTCAATTCACCTTTAGTGAAGACCCTCTAGGAGTAAG  
ATACTGTGGGAAAACAGATACCAATAAGTATATCATGCTTGCCCTAGAGAGTTTGCAATC  
TACCTAGAGAGAAAGGAAGGTGAACTTGAGAGATCTATATACATAGGTAAAGATTGTAG  
TGCATGGTTTTGAGGCACATTATCCCTACAACAAATTTTGATAACAGAAGAC

SEQ ID NO: 48\_AA435956\_H

ACTTTTACTATATTCTTTGAGATGACTGTTTTTTGATTTAGAGGCGAAATCAGCACGTGGT  
GGCTCAAATCTCCTTATGGATAGTGTTTCTTCCTTCCAGCTTTTTCATGTTTCAACTTTTG  
CGGGGCTGGCGTACATCCACCACCAACACGTTCTTCACAGGGACCTGAAACCTCAGAAC  
TACTCATCAGTCACCTGGGAGAGCTCAAACCTGGCTGATTTTGGTCTTGCCCGGGCCAAG  
TCCATTCCCAGCCAGACATACTCTTCAGAAGTCGTGACCCTCTGGTACCGGCCCCCTGAT  
GCTTTGCTGGGAGCCACTGAATATTCCTCTGAGCTGGACATATGGGGTGCAGGCTGCATC  
TTTATTGAAATGTTCCAGGGTCAACCTTTGTTTCTGGGGTTTCCAACATCCTTGAACAG  
CTGGAGAAAATCTGGGAGGTGCTGGGAGTCCCTACAGAGGATACTTGGCCGGGAGTCTCC  
AAGCTACCTAACTACAATCCAGAATGGTTCCCACTGCCTACGCCTCGAAGCCTTCATGTT  
GTCTGGAACAGGCTGGGCAGGGTTCTGAAAGCTGAAGACCTGGCCTCCCAGATGCTAAAA  
GGCTTTCCCAGAGACCGCGTCTCCGCCCAGGAAGCACTTGTTTCATGATTATTTTCAGCGCC  
CTGCCATCTCAGCTGTACCAGCTTCCTGATGAGGAGTCTTTGTTTACAGTTTCAGGAGTG  
AGGCTAAAGCCAGAAATGTGTGACCTTTTGGCCTCCTACCAGAAAGGTCACCACCCAGCC  
CAGTTTAGCAAATGCTGGTGAAAAGAAAGGGCGAGATCACCAAGGTTCTTCCAGGGCTGT  
ATTTCTGCAGTTTCGGTTTTTCATTTGCTTCAGCTTACTAAGAAGCTTCAAATCTAACTCC  
ATACTGAACAAGGGGCTTTATGTCCTCACCTATGACCTGGAATAGTTTAAATATGGTGTT  
CAAGGCAATAGTACATAATAGTGGAAGAAAATTCAGTGGAAGGTTATTGCTATTGTCATT  
TGCATAGAATTTAAGTGATTGATTTAAAAAACTGGACATAAACTAAGTCTAAGAAG

SEQ ID NO: 49\_AA626859\_H

AAATGGAGTTGCTGATGGAGTGATCAAAAGCGTATTATGGCAAACACTTCAAGCTCTTAA  
TTTCTGTCATATACATAACTGTATTCACAGAGATATAAAACCTGAAAATATTCTAATAAC  
TAAGCAAGGAATAATCAAGATTTGTGACTTCGGGTTTGCACAAATTCTGATTCCAGGAGA  
TGCCTACACCGATTATGTAGCTACGAGATGGTACCGAGCTCCTGAACCTTCTTGTGGGAGA  
TACTCAGTATGGTTCTTCAGTCGATATATGGGCTATTGGTTGTGTTTTTGCAGAGCTCCT  
GACAGGCCAGCCACTGTGGCCTGGAAAATCAGATGTGGACCAACTTTATCTGATAATCAG  
AACACTAGGAAAATTAATCCCAAGACATCAATCAATCTTTAAAAGTAACGGGTTTTTCCA  
TGGCATCAGTATACCTGAGCCAGAAGACATGGAACTCTTGAGGAAAAGTTCTCAGATGT  
TCATCCTGTGGCTCTGAACTTCATGAAGGGGTGTCTGAAGATGAATCCAGATGACAGATT  
AACCTGTTCCCAACTCCTGGAGAGCTCCTACTTTGATTCTTTTCAAGAGGCCCAAATTA  
AAGAAAAGCACGTAATGAAGGAAGAAACAGAAGACGCCAACAGAATCAACTGTTGCCTCT  
CATACCAGGAAGCCACATCTCCCCACACCTGATGGAAGAAAACAAGTCCTCCAGTTAAA  
ATTTGATCACCTTCCAAACATTTAGGAAAATGTTCTTTCAAGTGCAAAGTAATTTAATAT  
GTACACATTTTGTACAAGTGAGATAGGAATTCTCAGTGTTTCAAATGCAAATGAGCCATA

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## FIGURE 2NN

TGAAAATTAAGATGCCTTCTAGAATTGGTTTGCTCTGATCATTGGCTGATTCCCTTTCCCCA  
TGCTTTTACAT

SEQ ID NO: 50\_AA061797\_M

GAAAATAGCCCTGCGGGAAATCCGTATGCTGAAGTTGAAACACCCAAACCTCGTGAACCT  
CATCGAGGTGTTTCAGAAGAAAGAGAAAGATGCATCTAGTTTTTTGAGTACTGTGATCACAC  
ACTGTTAAACGAGCTGGAGAGAAACCCAAACGGAGTTTCTGATGGAGTGATTAAAAGTGT  
GCTATGGCAAACCCCTTCAAGCCCTTAACCTTCTGTCACAAGCACAATTGTATTCATCGGGA  
TGTAACCTGAAAACATCCTAATAACCAAGCAAGGGATGATAAAGATTTGTGACTTTGG  
ATTTGCACGAATTCTAATTCCAGGAGACGCCTACACAGACTATGTTGCCACCAGGTGGTA  
CCGAGCCCCCGAACTTCTCGTGGGAGACACGAAGTACGGTTCCTCTGTAGACGTGTGGGC  
CGTCGGCTGTGTTTTTGCAGAGCTCCTGACGGGTCAGCCACTCTGGCCGGGAAAATCCGA  
CGTGGACCAGCTTTACCTGATCATCAGGACGTTGGGGAAGCTGATTCCAAGACACCAGTC  
TATCTTTAGGAGTAACCAGTTTTTCCGCGGCATCAGCATACCTGAACCAGAGGACATGGA  
GACTCTTGAAGAAAAATTCTCAAATGTTTCAGCCTGTGGCTTTAAGTTTCATGAAGGGATG  
CCTGAAGATGAATCCTGATGAGAGGCTGACCTGTGCCCAGCTGCTGGACAGTGCCTACTT  
TGAGTCTTTTCAAGAGGATCAAATGAAAAGAAAAGCCCCGAGTGAGGGGAGAAGCCGAAG  
GCGCCAGCAGAATCAACTGCTGCCTCTTATTCCTGGAAGCCACATCTCCCCCACACCTGA  
TGGAAGGAAACAAGTCGTCCAGTTAAAGTTCGATCATCTTCCAAACATTTAGGGGACTCA  
TCCTTCCCAGCACATCCTTTTAATATTGTCTACATAGGAATAAGACGGGAATCCTCAGCA  
TCTCAAATACAGTGAGCGACGTGAACACCAGGGCACCTCTAATCACCACGGGCTCCTCCC  
CTGTGCTTTTTTCCACGCCAGCTCCATCTCCTAAAACATTCTCTTTAAATGTTGCAGTATC  
AAAATGGCACATCCGAAAGAGATGCTTCCAGTTTCACCAGAGCCGGGCTTCCTCAGGCAA  
TCGGTACTGTGCATCTGTGGACTTATGCTCCGACCTAGGGAAAGATTTCCACGTAGCCGT  
CTCACTTCAGCCGACCAGTGGTGTCTGAAGCAGACCCAGATCTGCTGGCTGCTGTTTGT  
GGAGGGGATGGCCCTGAGCCCTCTCACTGGAGTTTCTTCTCCGTGCAGCCAGGTCTTACT  
TTAGACTACATTTGTGTTATTGTGGCATGGCAATCGTGAAAGGTGGTCTAGGTTTACCCT  
TGACTCCACAGCAGATGCTAGTCTCCTTCTCGTGAGGAGCTGACAAGTCTGCTTCTAAAA  
CGAACTAGAGAAAATTCCAAACGTGACCAGTTAGTGGACAGACTACAAGGAATCGACCAC  
CATACCACAGTAACGCCCCCTGGATCCCTGGCTGCCCACCCACTCTAAGGCTATCCTGGTT  
CACCATGGTTTCTCTTTCTTTTCTTCTTTTTTAATCTATTTGTACATATGAGAAAGAGGC  
AGAGGGGCGAGAGAAACCTCGTGTGTGAAAATCAAAGACAAGCAGGAGGCCAGCCTAAG  
CTACATAGCAAGGCCTTTTCTCTACACCCATTCTCTAAGGTTGCTTAAACCCAAAGTCCCT  
GCTGCTGATTGTATAAACTATGAATAAGTTCTACATATGTAGGACATATTGTTGTCATTG  
TTGAAATATCTAAGGATCTTGGTAGAAGCAGAAGTGTTCTAAATATTCTCCACACTGGTG  
AGTATCTTGGCATTTTCATTTCTGACCTCATCACAGATGAACACATCAAAGGATGAGTATG  
TATCACTTTGCATCTTAGAATTCTACCTGTTTTAGCTGCGTTAAACCTTGTGAAAGGGCG  
GGGCCATAACTGAACCTGTGGAGTTCTTGCTGTGTGCAGGAAACCCCTCTGGTTTTGTCT  
CCAGCATGGAAGAAAACAGCTATAGTCACACCTACCTGAAAGTAGAAATTCAAAGTCACT  
GTCCTTGACTACATATGCAGTCCAAGGCCACGCTGGGCTACACTTCTCCAGGCATGAAGG  
TCCGTGTTTTGTATCAAGGGGCAGGAAAGGAGAGTCCAAGGTCAAGGCCAGCCGAGGCTGC  
ATAGTGAGTTGAGGCTCTTCAGCAAAAGAAAAGCAAACATAATAGGAGTCGTTGAAGGTAG  
CCACCGGCCATTTCTCTAAATATCATTCTGCTGAAAAGGGGGCTTAGTTTAGTTTAGAAT  
GCATTAATGTATGTAGAAGCTGGGCTATTTTCAGATTATTTGAAATTGTAGCTATTGTTAA  
TTAGCACTTAATAACTAAGTATTATGGTAGTCTAAACTATTAGAGTTTACTACAAAG  
AGGTTTTGATTGAATTATATTAACATATAATATGGATTTTAAAAATTTAAGATGTTTAA  
GAAAGCTATATAAAGATTAAACATTTTTGTGGCTGTATATTTGTGTATATACCTTGGTTG  
TTCTTTAAATTATTTTAATAAAAGCCAGAAACATT

## FIGURE 200

SEQ ID NO: 51\_AA397553\_H

ATGCCCAATTCAGAGAGACATGGGGGCAAGAAGGACGGGAGTGGAGGAGCTTCTGGAAC  
TTGCAGCCGTCATCGGGAGGCGGCAGCTCTAACAGCAGAGAGCGTCACCGCTTGGTATCG  
AAGCACAAGCGGCATAAGTCCAAACACTCCAAAGACATGGGGTTGGTGACCCCCGAAGCA  
GCATCCCTGGGCACAGTTATCAAACCTTTGGTGGAGTATGATGATATCAGCTCTGATTCC  
GACACCTTCTCCGATGACATGGCCTTCAAACCTAGACCGAAGGGAGAACGACGAACCTCGT  
GGATCAGATCGGAGCGACCGCCTGCACAAACATCGTCACCACCAGCACAGGCGTTCCCGG  
GACTTACTAAAAGCTAAACAGACCGAAAAAGAAAAAGCCAAGAAGTCTCCAGCAAGTCG  
GGATCGATGAAGGACCGGATATCGGGAAGTTCAAAGCGTTCGAATGAGGAGACTGATGAC  
TATGGGAAGGCGCAGGTAGCCAAAAGCAGCAGCAAGGAATCCAGGTCATCCAAGCTCCAC  
AAGGAGAAGACCAGGAAAGAACGGGAGCTGAAGTCTGGGCACAAAGACCGGAGTAAAAGT  
CATCGAAAAAGGGAAACACCCAAAAGTTACAAAACAGTGGACAGCCCAAACCGGAGATCC  
AGGAGCCCCCACAGGAAGTGGTCTGACAGCTCCAAACAAGATGATAGCCCCCTCGGGAGCT  
TCTTATGGCCAAGATTATGACCTTAGTCCCTCACGATCTCATACTCGAGCAATTATGAC  
TCCTACAAGAAAAGTCCTGGAAGTACCTCGAGAAGGCAGTCGGTCAGTCCCCCTTACAAG  
GAGCCTTCGGCCTACCAGTCCAGCACCCGGTCACCGAGCCCCCTACAGTAGGCGACAGAGA  
TCTGTCAGTCCCTATAGCAGGAGACGGTCGTCCAGCTACGAAAGAAGTGGCTCTTACAGC  
GGGCGATCGCCCAGTCCCTATGGTCGAAGGCGGTCCAGCAGCCCTTTCCTGAGCAAGCGG  
TCTCTGAGTCGGAGTCCACTCCCCAGTAGGAAATCCATGAAGTCCAGAAGTAGAAGTCCT  
GCATATTCAAGACATTCATCTTCTCATAGTAAAAAGAAGAGATCCAGTTCACGCAGTCGT  
CATTCCAGTATCTCACCTGTCAGGCTTCCACTTAATTCCAGTCTGGGAGCTGAACTCAGT  
AGGAAAAAGAAGGAAAGAGCAGCTGCTGCTGCTGCAGCAAAGATGGATGGAAAGGAGTCC  
AAGGGTTCACCTGTATTTTTGCCTAGAAAAGAGAACAGTTCAGTAGAGGCTAAGGATTCA  
GGTTTGGAGTCTAAAAAGTTACCCAGAAGTGTAATAATTGGAAAAATCTGCCCCAGATACT  
GAACTGGTGAATGTAACACATCTAAACACAGAGGTAAAAAATTCTTCAGATACAGGGAAA  
GTAAAGTTGGATGAGAACTCCGAGAAGCATCTTGTTAAAGATTTGAAAGCACAGGGAAACA  
AGAGACTCTAAACCCATAGCACTGAAAGAGGAGATTGTTACTCCAAAGGAGACAGAAACA  
TCAGAAAAGGAGACCCCTCCACCTCTTCCCACAATTGCTTCTCCCCCACCCTCTACCA  
ACTACTACCCCTCCACCTCAGACACCCCTTTGCCACCTTTGCCTCCAATACCAGCTCTT  
CCACAGCAACCACCTCTGCCTCCTTCTCAGCCAGCATTTAGTCAGGTTCTTGCTTCCAGT  
ACTTCAACTTTGCCCCCTTCTACTCACTCAAAGACATCTGCTGTGTCCTCTCAGGCAAAT  
TCTCAGCCCCCTGTACAGGTTTCTGTGAAGACTCAAGTATCTGTAACAGCTGCTATTCCA  
CACCTGAAAACCTTCAACGTTGCCTCCTTTGCCCTCCACCCCTTATTACCTGGAGGTGAT  
GACATGGATAGTCCAAAAGAACTCTTCCTTCAAACCTGTGAAGAAAGAGAAGGAACAG  
AGGACACGTCACCTTACTCACAGACCTTCCTCTCCCTCCAGAGCTCCCTGGTGGAGATCTG  
TCTCCCCCAGACTCTCCAGAACCAAAGGCAATCACACCACCTCAGCAACCATATAAAAAG  
AGACCAAAAATTTGTTGTCCTCGTTATGGAGAAAGAAGACAAACAGAAAGCGACTGGGGG  
AAACGCTGTGTGGACAAGTTTGACATTATTGGGATTATTGGGAGAAGGAACCTATGGCCAA  
GTATATAAAGCCAGGGACAAAGACACAGGAGAACTAGTGGCTCTGAAGAAGGTGAGACTA  
GACAATGAGAAAGAGGGCTTCCCAATCACAGCCATTTCGTGAAATCAAATCCTTCGTCAG  
TTAATCCACCGAAGTGTTGTTAACATGAAGGAAATTGTCACAGATAAACAAGATGCACTG  
GATTTCAAGAAGGACAAAGGTGCCTTTTACCTTGTATTTGAGTATATGGACCATGACTTA  
ATGGGACTGCTAGAATCTGGTTTGGTGCACCTTTTCTGAGGACCATATCAAGTCGTTTCATG  
AAACAGCTAATGGAAGGATTGGAATACTGTCACAAAAAGAATTTCTGTCATCGGGATATT  
AAGTGTTCTAACATTTTGCTGAATAACAGTGGGCAAATCAAACCTAGCAGATTTTGGACTT  
GCTCGGCTCTATAACTCTGAAGAGAGTCGCCCTTACACAAACAAAGTCATTACTTTGTGG  
TACCGACCTCCAGAACTACTGCTAGGAGAGGAACGTTACACACCAGCCATAGATGTTTGG  
AGCTGTGGATGTATTCTTGGGGAAGTATTCACAAAGAAGCCTATTTTTCAAGCCAATCTG  
GAACTGGCTCAGCTAGAACTGATCAGCCGACTTTGTGGTAGCCCTTGTCCAGCTGTGTGG  
CCTGATGTTATCAAACCTGCCCTACTTCAACACCATGAAACCGAAGAAGCAATATCGAAGG

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## FIGURE 2PP

CGTCTACGAGAAGAATTCTCTTTCATTCCTTCTGCAGCACTTGATTTATTGGACCACATG  
CTGACACTAGATCCTAGTAAGCGGTGCACAGCTGAACAGACCCTACAGAGCGACTTCCTT  
AAAGATGTCGAACTCAGCAAAATGGCTCCTCCAGACCTCCCCCACTGGCAGGATTGCCAT  
GAGTTGTGGAGTAAGAAACGGCGACGTCAGCGACAAAGTGGTGTGTAGTCGAAGAGCCA  
CCTCCATCCAAAACCTTCTCGAAAAGAACTACCTCAGGGACAAGTACTGAGCCTGTGAAG  
AACAGCAGCCCAGCACCACTCAGCCTGCTCCTGGCAAGGTGGAGTCTGGGGCTGGGGAT  
GCAATAGGCCTTGCTGACATCACACAACAGCTGAATCAAAGTGAATTGGCAGTGTTATTA  
AACCTGCTGCAGAGCCAAACCGACCTGAGCATCCCTCAAATGGCACAGCTGCTTAACATC  
CACTCCAACCCAGAGATGCAGCAGCAGCTGGAAGCCCTGAACCAATCCATCAGTGCCCTG  
ACGGAAGCTACTTCCCAGCAGCAGGACTCAGAGACCATGGCCCCAGAGGAGTCTTTGAAG  
GAAGCACCTCTGCCCCAGTGATCCTGCCTTCAGCAGAACAGATGACCCTTGAAGCTTCA  
AGCACACCAGCTGACATGCAGAATATATTGGCAGTTCTCTTGAGTCAGCTGATGAAAACC  
CAAGAGCCAGCAGGCAGTCTGGAGGAAAACAACAGTGACAAGAACAGTGGGCCACAGGGG  
CCCCGAAGAACTCCCACAATGCCACAGGAGGAGGCAGCAGCATGTCTCCTCACATTCTT  
CCACCAGAGAAGAGGGCCCCCTGAGCCCCCGGACCTCCACCGCCGCCACCTCCACCCCCCT  
CTGGTTGAAGGCGATCTTTCCAGCGCCCCCAGGAGTTGAACCCAGCCGTGACAGCCGCC  
TTGCTGCAACTTTTATCCCAGCCTGAAGCAGAGCCTCCTGGCCACCTGCCACATGAGCAC  
CAGGCCTTGAGACCAATGGAGTACTCCACCCGACCCCGTCCAAACAGGACTTATGGAAAC  
ACTGATGGGCCTGAAACAGGGTTCAGTGCCATTGACACTGATGAACGAACTCTGGTCCA  
GCCTTGACAGAATCCTTGGTCCAGACCCTGGTGAAGAACAGGACCTTCTCAGGCTCTCTG  
AGCCACCTTGGGGAGTCCAGCAGTTACCAGGGCACAGGGTCAGTGACGTTTCCAGGGGAC  
CAGGACCTCCGTTTTTGCCAGGGTCCCCTTAGCGTTACACCCGGTGGTCGGGCAACCATTC  
CTGAAGGCTGAGGGAAGCAGCAATTCTGTGGTACATGCAGAGACCAAATTGCAAACTAT  
GGGGAGCTGGGGCCAGGAACCACTGGGGCCAGCAGCTCAGGAGCAGGCCTTCACTGGGGG  
GGCCCAACTCAGTCTTCTGCTTATGGAAAACCTCTATCGGGGGCCTACAAGAGTCCCACCA  
AGAGGGGGAAGAGGGAGAGGAGTTCCTTACTAA

SEQ ID NO: 52\_AA789239\_H

TGAAAATGGAGATGTATGAAACCTTGGAAAAGTGGGAGAGGGGAAGTTACGGAACAGTCA  
TGAAATGTAAACATAAGAATACTGGGCAGATAGTGGCCATTAAGATATTTTATGAGAGAC  
CAGAACAATCTGTCAACAAAATTGCGATGAGAGAAATAAAGTTTCTAAAGCAATTTTCATC  
ACGAAAACCTGGTCAATCTGATTGAAGTTTTTAGACAGAAAAAGAAAATTCATTTGGTAT  
TTGAATTTATTGACCACACAGTATTAGATGAGTTACAACATTATTGTTCATGGACTAGAGA  
GTAAGCGACTTAGAAAATACCTCTTCCAGATCCTTCGAGCAATTGACTATCTTCACAGTA  
ATAATGTAATCATTCATCGAGATATAAAACCTGAGAATATTTTAGTATCCCAGTCAGGAA  
TTACTAAGCTCTGTGATTTTGGTTTTTGCACGAACACTAGCAGCTCCTGGGGACATTTATA  
CGGACTATGTGGCCACACGCTGGTATAGAGCTCCCGAATTAGTATTAAAAGATACTTCTT  
ATGGAAAGTATGTGCCTGTGGATATCTGGGCTTTGGGCTGTATGATCATTGAGATGGCCA  
CTGGAAATCCCTATCTTCCTAGTAGTTCTGATTTGGATTTACTCCATAAAATTGTTTTGA  
AAGTGNGATTCTATGCCAGAACTGAAAGCTAAATTACTGCAGGAAGCAAAAGTCAATTCAT  
TAATAAAGCCAAAAGAGAGTTCTAAAGAAAATGAACTCAGGAAAGATGAAAGAAAAACAG  
TTTATACCAATACACTGCTAAGTAGTTTCAGTTTTTGGGAAAGGAAATAGAAAAAGAGAAA  
AGCCCAAGGAGATCAAAGTCAGAGTTATTAAAGTCAAAGGAGGAAGAGGAGATATCTCAG  
AACCAGAAAAGAGAGTATGAAGGTGGACTTGGTCAACAGGATGCAAAATGAAAATGTTC  
ATCCTATGTCTCCAGATACAAAACCTTGTAACCATTTGAACCAACCAACCCCTATCAATCCCA  
GCACTAACTGTAATGGCTTGAAAGAAAATCCACATTGCGGAGGTTCTGTGACAATGCCAC  
CCATCAATCTAACTAACAGTAATTTGATGGCTGCAAATCTCAGTTCAAATCTCTTTCACC  
CCAGTGTGAGGTAACTGAAAGAGCAAAAAAGAGACGCACTTCTTCACAATCTATTGGAC  
AAGTTATGCCTAATAGCAGGCAAGAGGATCCAGGTCCTATTCAAAGCCAAATGGAGAAGG  
GTATATTTAATGAGCGAACAGGTACAGTGACCAAATGGCAAATGAGAACAAGGAAGC

## FIGURE 2QQ

TGAATTTTCCAGATCTGACAGGAAAGAATTCCATTTTCCAGAATTGCCTGTCACAATAC  
AGTCAAAAGATACAAAAGGAATGGAAGTTAAACAGATAAAAATGCTGAAGAGGGAGTCAA  
AGAAAACAGAGTCATCTAAGATACCAACTTTACTTAACGTGGATCAAAATCAAGAAAAC  
AAGAGTTTATTCCCTTATCTCTGCTGTCTGCCTGCTGTCCTATTTTCACAAATATTTGCT  
CTCAGCTAACTATCAGGGTGGAGATGGCCATTGCGAGGGGAAGAATTTGAAGAGAAACAG  
GTTTTTTTTCTGGTAGTGTCTTTTCTTTTACATAGTCCAAAAAATACAAGATGACAACTC  
TTCCCGTTTTTATTTATCTACAATAGAAGTGTGATGTGAGTTGTTGTTAAGACAGCCATCC  
ATGTGCATGAGCATCATCCAGCTTTTTTTTGTAGCAAAACATTTACTGTTTTTCTTTTCCC  
TTTTAAGACTCTGTTGATGTGATAATTTGATTTGGAATTATAAAGTCATCTCTTCTCTGC  
CTTGAA

SEQ ID NO: 53\_AA124976\_M

CTGGCAGATATAGTTCATGCTTGTTTACAAATTGATCCTGCTGAGAGGACATCATCTACT  
GATCTTTTGCCTCACGATTACTTTACTAGAGATGGATTTATTGAGAAATTCATACCAGAG  
CTGAGAGCTAAATTATTACAGGAAGCAAAGGTTAATTCATTTATAAAGCCAAAAGAGAAT  
TTTAAAGAAAATGAACCTGTGAGAGATGAGAAGAAATCAGTTTTTACCAACACCCTGCTC  
TATGGAAATCCATCACTTTATGGCAAGGAAGTGGACAGAGACAAAAGGGCCAAGGAGCTC  
AAAGTCAGAGTCATTAAGGCCAAAGGGGGCAAAGGAGATGTCCCAGACCAGAAGAAGCCA  
GAGTATGAAGGCGACCACCGCCAGCAGGGCACAGCTGATGACACACAGCCCTCATCACTG  
GACAAGAAGCCTTCTGTCTTGGAAGTACAAACCCCTCTCAATCCCAGTGAGAATTCTGAC  
GGTGTCAAAGAAGACCCACACGCTGGGGGTGTATGATAATGCCACCTATCAACCTGACA  
AGCAGTAATTTGTTGGCCGCAAATCTCAGTTCAAACCTTTCCCACCCCAATTCACGGTTA  
ACTGAAAGAACAAAAAGAGACGCACTTCTTCACAACTATTGGACAGACTTTGTCTAAT  
AGCAGACAAGAGGACACAGGTCCACACAAGTCCAAACAGAGAAAGGTGCATTTAATGAG  
CGAACAGGTCAGAATGACCAAATATCGAGTGGGAACAAAAGAAAGCTGAATTTTCCCAA  
TGCGACAGGAAAGAATTCCATTTCCCTGAACTGCCATTACAGTGCAGGCGAAGGAGATG  
AAAGGGATGGAAGTTAAACAGATAAAAGTGCTGAAGAGAGAATCAAAGAAAACAGATTCA  
TCTAAAATACCAACTTTACTTAGTATGGACCCAAATCAAGAAAAACAAGAGGGTGGAGAT  
GGCGATTGTGAGGGGAAGAATTTGAAGAGGAACAGATTTTTTTTTTTTCCCGATAGTGCTTT  
GTCTTTTAAGTAATCTTAAAAATACAAGCTTGACAATTCCTTCCTTTTTTATTTTATATAC  
ACTAGAATGTACATAGGTTGCTGCTAAGATAGCCACCCATCCCATCTGCATCAACATCAT  
CTATTTTTTTTGGTTTTTGCTAGCAAAATTTTCACAATTTTTTCTCTATCTTCCAAAACTGT  
TATTTTGATGCTGTGATTTGAAATTATAAAGTCACCTCCTCTGTCTGCTTCCTTCCTTGC  
CATGATTACTGAGTGGGTAGTCACATGATGTGCCCTGCTCGCACTGCTCTCAGACTGCTG  
AGACTCAAACCTCATAAGCCAGGGGTCTCCTGGGAAGCACTGGCCTCTTCAAGTGGATGC  
TCGATGAACCTTCTTATCTGTTGTCTTAGTAACCACTCGTTGCCATCACATGATGAAAGA  
CATTCTATTGTCCCCAGTGAAGCATTTATAGTACTTACATAACATGTTACAGTGATATGA  
TGTTCCTAGGTTAAACTCCTTGAGATGAACTATTTCCCTGCATTCTCTGACTCCCCTAGT  
CTAATAGTTCCCTCCATTTAGCCAGAAGAATTTCCCTGAAGAAGCGATGCACAACCTGGGA  
AAGGTTTACTTTCTATCCTGGGCTGTTTTCTGTTGCTAAATAATATAGACTGGGTAGTTA  
GTTAACAT

SEQ ID NO: 54\_AA575635\_M CCRK\_M

AGCGCTCAGGCCAGCTCAAGATAGCTGACTTTGGCCTGGCCCGGGTCTTCTCTCCGGAT  
GGTGGTCGCCTCTACACACATCAGGTGGCCACCAGGTGGTACCGAGCTCCTGAACTCCTG  
TATGGCGCTCGGCAGTATGACCAGGGCGTTGACCTATGGGCTGTGGGCTGCATCATGGGA  
GAGCTGTTGAATGGGTCCCCCTGTTCCCGGGCGAAAACGACATTGAACAACCTGTGCTGT  
GTGCTTCGCATCCTGGGTACCCCGAGTCCTCGAGTCTGGCCGGAGATCACAGAGCTGCCT  
GACTACAACAAGATCTCCTTCGAGGAGCAGGCACCAGTGCCCTGGAGGAGGTGCTGCCT  
GATGCCTCTCCCCAGGCCTTGGACCTGCTGGGCCAGTTCCTCCTCTACCCTCCACGACAG

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## FIGURE 2RR

CGTATTGCAGCCTCCCAGGCCCTTCTGCATCAGTACTTCTTCACAGCGCCTCTGCCTGCC  
CATCCATCCGAGCTGCCAATTCCTCAGCGCCCAGGGGGACCTGCACCCAAGGCTCACCCA  
GGGCCCCCCCCATGTCCACGACTTCCATGTGGATCGACCTATTGAGGAGTCACTGTTGAAC  
CCAGAACTGATTCCGGCCCTTCATCCCAGAGGGGTGAGATGCTGGTCCAGGCCTTCCTGCT  
CGCCCTAGGAGCACCTCTTTCTGATTTGCCTCCATGGCCTCCCCACGGCTATATATACCA  
CACCTGGTCCTGCTCCTGAGTGTGCTTGAGGGCTGGGCTCTGGGAGGCAGAACCGTGAGA  
TGTTTCATCCCAGCAGAGAAAGAGACTCACGTCCTACAGACAAAGCCTCCAGAAACTGCTA  
GCTGTGTCTTCTCCAGGGCCACCCCTCAGTGGTGCCACCCGGCCTTAGAGATGATTGTC  
AGGCTCTGTCCCCTCTTCAAGGACATTGGTACTACAGCACCACCTGGTGGAAGCACAGAG  
TATAAGCTGTCTTCATACTGGGGACACAGCTGGGAAGTCAGACATGTTTTAGTTTTGGTT  
CCACTGGGTCAGGATTTGAGGTTTCATATAAAAGCCCTGGGTGTTTTCTGTCTAATTGCACC  
TTGTCTGTTGCTGTTAGGGAAAGGACAATGGTGGGCCTTGATTCACAGGGGTCAGGTACT  
CAGAAGGGGCCTCCTGTGAAGGCCATTTGGGTCTCAGGCTTCCCATGCTATTCACGGGA  
CTTGAGTGCTCATTTGGGAGCGAGGGTCCAGAAGCTGAGGCCCAGGGATGGACAGTCCAG  
TTCCCGAAGCCCACTTCCCACATGTCTGGGTGGGTGAGTCAGTGAGCCTGAGGCTGCCTTG  
CAGATGCGGAAGCAGGCATTCTGGAATCCACTCAGTAAATAAATTCCAGTGTGACTCAG

SEQ ID NO: 55\_AA631990\_H

GAACAACAATAACAGAATAAGGAAGAAAATCTCATGATTACCTCAATAAGTACAGAGAAA  
TCTGGTCACACTCACTATCCATTTCATGATTACAACCTCTTCAATACTATCGCGGCCGAGGA  
GGGAAGACGGCAGTTTGGCGACATTTCTCGGCCGAAGGGCCATTTGCTTTTGCGGAGATG  
CGGCATTCCAAAAGAACTCACTGTCCTGATTGGGATAGCAGAGAAAGCTGGGGACATGAA  
AGCTATCGTGGAAGTCACAAGCGGAAGAGGAGATCTCATAGTAGCACACAAGAGAACAGG  
CATTGTAAACCACATCACCAGTTTAAAGAATCTGATTGTCAATTATTTAGAAGCAAGGTCC  
TTGAATGAGCGAGATTATCGGGACCGGAGATACGTTGACGAATACAGGAATGACTACTGT  
GAAGGATATGTTCTTAGACATTATCACAGAGACATTGAAAGCGGGTATCGAATCCACTGC  
AGTAAATCTTCAGTCCGCAGCAGGAGAAGCAGTCCTAAAAGGAAGCGCAATAGACACTGT  
TCAAGTCATCAGTCACGTTTCGNATGAAATCGTGGACACTTTGGGTGAAGGAGCCTTTGGC  
AAAGTTGTAGAGTGCATTGATCATGGCATGGATGGCATGCATGTAGCAGTGAAAATCGTA  
AAAAATGTAGGCCGTTACCGTGAAGCAGCTCGTTTCAGAAATCCAAGTATTAGAGCACTTA  
AATAGTACTGATCCCAATAGTGTCTTCCGATGTGTCCAGATGCTAGAATGGTTTGATCAT  
CATGGTCATGTTTGTATTGTGTTTGAACACTACTGGGACTTAGTACTTACGATTTTCATTAAA  
GAAAACAGCTTTCTGCCATTTCAAATTGACCACATCAGGCAGATGGCGTATCAGATCTGC  
CAGTCAATAAATTTTTTACATCATAATAAATTAACCCATACAGATCTGAAGCCTGAAAAT  
ATTTTGTGTTGTGAAGTCTGACTATGTAGTCAAATATAATTCTAAAATGAAACGTGATGAA  
CGCACACTGAAAAACACAGATATCAAAGTTGTTGACTTTGGAAGTGCAACGTATGATGAT  
GAACATCACAGTACTTTGGTGTCTACCCGGCACTACAGAGCTCCCGAGGGTCATTTTGGCT  
TTAGGTTGGTCTCAGCCTTGTGATGTTTGGAGCATAGGTTGCATTCTTATTGAATATTAC  
CTTGGTTTCACAGTCTTTTCAGACTCATGATAGTAAAGAGCACCTGGCAATGATGGAACGA  
ATATTAGGACCCATACCACAACACATGATTCAGAAAACAAGAAAACGCAAGTATTTTCAC  
CATAACCAGCTAGATTGGGATGAACACAGTTCTGCTGGTAGATATGTTAGGAGACGCTGC  
AAACCGTTGAAGGAATTTATGCTTTGTTCATGATGAAGAACATGAGAACTGTTTGACCTG  
GTTCTGAAGAATGTTAGAATATGATCCAACTCAAAGAATTACCTTGGATGAAGCATTGCAG  
CATCCTTTCTTTGACTTATTAAAAAAGAAATGAAATGGGAATCAGTGGTCTTACTATATA  
CTTCTCTAGAAGAGATTACTTAAGACTGTGTCAGTCAACTAAACATTCTAATATTTTTGT  
AAACATTAAATTATTTTGTACAGTTAAGTGTAATATTGTATGTTTTGTATCAATAGCAT  
AATTAAGTTGTTAAGCAAGTATGGTCTTGATAATGCATTAGAAAAATTAAATTAATTTT  
TCTTTTTGAAATTACCATTTTTTAAATACCTTTGAAATATCCTTTGTGTCCAGTGATAAAT  
GTGATTGATCTTGCCTTTTGTACATGGAGGTCACCTCTGAAGTGATTTTTTTTTGAGTAAA  
AGGAAATCTTGACTACTTTATATTCTTAAAGGAATATTCTTTATATACTTCAAATTTAGA



## FIGURE 2SS

ACTTAACTTTAAAAGTTTTTCTTCTGTAATTGTTGAACGGGTGATTATTATTAACCTCTAG  
ATAAGCAGGTACTAGAAACCAAACTCAGAAAATGTTTACTGTTAGAATTCTATTAAATT  
TTAAGTGTTGTATTCTTTTTTCATTGGGTGATGTCAGGGTGATAACCAGACATTCATGGAA  
AGGCATGCAGTTTGTCCATTGTGACAGTTTGTTTAATAAAAACCAACATACACACTTTATTT  
AAGATTAATAATCTAACTGGAAAGTCAGCTTGGAAAATGGACATTTCCAAGTATGTTTGGT  
GAGTCACAGATATAAAAATAGAAATTCTGATGAGAGGTTTCAGTTTTTAATACCAAGTCC  
TTAGGAGTCTTAACATTGGCCAGCATCTGTTTATCAAATGACATAAATACGTAAACCTAT  
AAGAATTAAGTTTATTAATTAGGCAATTTATGTCTGTGATAATTCTTACGGGAGAAAGAG  
GATTTGATTGGAAAGCAGTTTGGGAAGAAAGTGCTGCTGAAATTTCCAGAATTTAATTGA  
TTGGTTACATAAACTTTTTGACTTCAAT

SEQ ID NO: 56\_AA557536\_H

AGTAAGGCCCCGCGGGCGTCCTGGCCGCCATGTGCACCGTAGTGGACCCTCGCATTGTCC  
GGAGATACCTACTCAGGCGGCAGCTCGGGCAGGGGAGAACATTCCGGGAAATCACGCTCC  
TCCAGGTGAGTGGCCTGGGCCCCTCCAGTCCAATCCCCTTGCCCAGGTACAGATCTCTCCA  
GACAGGAGAGAACTGGCCTTCTTGGGCCCCAGAGCACAGCCCCCTCCTGGCCTTCCAGCC  
GCCTCCGACTCTCTCCCCAGGAGTTTGGGGACCATCCCAACATCATCAGCCTCCTTGACG  
TGATCCGGGCAGAGAACGACAGGGACATTTACCTGGTGTTTGAGTTTATGGACACTGACC  
TGAACGCAGTCATCCGGAAGGGCGGCCTGCTGCAGGACGTCCACGTGCGCTCCATCTTCT  
ACCAGCTCCTGCGGGCCACCCGGTTCCTCCACTCGGGGCACGTTGTGCACCGGGACCAGA  
AGCCGTCCAATGTGCTCCTGGATGCCAACTGCACAGTGAAGCTGTGTGACTTTGGCCTGG  
CCCGCTCCCTGGGCGACCTCCCTGAGGGGCCTGAGGACCAGGCCGTGACAGAGTACGTGG  
CCACACGCTGGTACCGAGCACCGGAGGTGCTGCTCTCTTCGCACCGCTACACCGCTTCCT  
GCCCCAGATACACCCTTGGGGTGACATGTGGAGTCTGGGCTGTATCCTGGGGGAGATGC  
TGCGGGGGAGACCCCTGTTCCCCGGCACGTCCACCCTCCACCAGCTGGAGCTGATCCTGG  
AGACCATCCCACCGCCATCTGAGGAGXXXAGGCCACGACAGACGCTGGATGCCCTCCTAC  
CGCCAGACACCTCCCCAGAGGCCTTGGACCTCCTTAGGCGACTCCTGGTGTTTCGCCCCGG  
ACAAGCGGTTAAGCGCGACCCAGGCACTGCAGCACCCCTACGTGCAGAGGTTCCACTGCC  
CCAGCGACGAGTGGGCACGAGAGGCAGATGTGCGGGCCCCGGGCACACGAAGGGGTCCAGC  
TCTCTGTGCCTGAGTACCGCAGCCGCGTCTATCAGATGATCCTGGAGTGTGGAGGCAGCA  
GCGGCACCTCGAGAGAGAAGGGCCCCGGAGGGTGTCTCCCCAAGCCAGGCACACCTGCACA  
AACCCAGAGCCGACCCTCAGCTGCCTTCTAGGACACCTGTGCAGGGTCCCAGACCCAGGC  
CCCAGAGCAGCCCAGGCCATGACCCTGCCGAGCACGAGTCCCCCGTGCAGCCAAGAACG  
TTCCCAGGCAGAACTCCGCTCCCCTGCTCCAACTGCTCTCCTAGGGAATGGGGAAAGGC  
CCCCTGGGGCGAAGGAAGCGCCCCCTTGACACTCTCGCTGGTGAAGCCAAGCGGGAGGG  
GAGCTGCGCCCTCCCTGACCTCCCAGGCTGCGGCTCAGGTGGCCAACCAGGCCCTGATCC  
GGGGTGACTGGAACCGGGGCGGTGGGGTGAGGGTGGCCAGCGTACAACAGGTCCCTCCCC  
GGCTTCCTCCGGAGGCCCCGGCCCGGAGGATGTTACGACCTCTGCCTTGAGGGTG  
CCCAGGGGGGTGCCAGGGCTTTGCTTGGAGGCTACTCCCAAGCCTACGGGACTGTCTGCC  
ACTCGGCACTGGGCCACCTGCCCCCTGCTGGAGGGGCACCATGTGTGAGCCGCCCTACTCC  
CTTACCTGGCCCTCTGTTCCCTGCCCCAGCNCCTTCCCCAGACCCCTCTCCAGTCTCCTG  
CACCCCTTAGCCCTCCCTGCTTTGCCTGGCCCGTTGAAGTTCCAGGGAGCTTGCCCCGGGT  
CTCCTCGGGGGAGCAGATGAGGGCCCTGCCC

SEQ ID NO: 57\_N28606\_H, MOK\_H

ATGAAGAACTATAAAGCAATTGGCAAAATAGGAGAGGGGAACGTTTTCTGAAGTTATGAAG  
ATGCAAAGCCTGAGAGATGGAACTACTATGCATGTAAACAAATGAAGCAGCGCTTTGAA  
AGTATTGAGCAAGTCAACAACCTACGAGAGATCCAAGCACTGAGGCGCCTGAATCCGCAC  
CCAAACATTCTTATGTTGCATGAAGTGGTTTTTGACAGAAAATCTGGTTCTCTTGCACTA  
ATATGTGAACCTTATGGACATGAATATTTATGAGCTAATACGAGGGAGAAGATACCCATTA

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## FIGURE 2TT

TCAGAAAAAAATTATGCACTATATGTACCAAGTTATGTAAGTCCCTGGATCATATTCA  
AGAAATGGAATATTTTCACAGAGATGTAAAAACAGAAAAATATACTAATAAAGCAGGATGT  
CTGAAATTAGGGGACTTTGGCTCCTGCGGGAGTGTCTATTCCCAAGCAGCCGTACACGGAA  
TACATCTCCACCCGCTGGTACCGGGCCCCGGAGTGTCTCCTCACTGATGGGTTCTACACG  
TACAAGATGGACCTGTGGAGCGCGCGCTGTGTGTCTTCTACGAGATCGCCAGTCTGCAGCCC  
CTCTTTTCTGGAGTAAATGAACTGGACCAATCTCAAAAAATCCACGATGTTCATCGGCACA  
CCCGCTCAGAAGATCCTCACCAGTTCAACAGTCCGAGAGCTATGAATTTTGATTTTCTCT  
TTTAAAAAGGGATCAGGAATACCTCTACTAACAACCAATTTGTCCCCACAATGCCTCTCC  
CTCCTGCACGCAATGGTGGCCTATGATCCCGATGAGAGAATCGCCGCCCCACCAGGCCCTG  
CAGCACCCCTACTTCCAAGAACAGAGGAAAACAGAGAAGCGGGCTCTGGGCAGCCACAGA  
AAAGCTGGCTTTCCGGAGCACCCCTGTGGCACCGGAACCACTCAGTAACAGCTGCCAGATT  
TCCAAGGAGGGCAGAAAGCAGAAACAGTCCCTAAAGCAAGAGGAGGACCGTCCCAAGAGA  
CGAGGACCGGCCTATGTTCATGGAACCTGCCCAAATAAGCTTTTCGGGAGTGGTTCAGACTG  
TCGTCTTACTCCAGCCCCACGCTGCAGTCCGTGCTTGGATCTGGAACAAATGGAAGAGTG  
CCGGTGCTGAGACCCCTTGAAGTGCATCCCTGCGAGCAAGAAGACAGATCCGCAGAAGGAC  
CTTAAGCCTGCCCCGCAGCAGTGTGCTCTGCCACCATAGTGCGGAAAAGCGGAAGATAA

SEQ ID NO: 58\_AB023153\_H, ICK\_H

ATGAATAGATACACAACAATCAGGCAGCTCGGGGATGGAACCTACGGTTCCGTCTCTGCTG  
GGAAGAAGCATTGAGTCTGGGGAGCTGATCGCTATTAAAAAAATGAAAAGAAAATTTTAT  
TCCTGGGAGGAATGCATGAACCAACGGGAGGTTAAGTCTTTAAAGAAGCTCAACCATGCC  
AATGTAGTCAAATTAAGAAGTTATCAGGGAAAATGATCATCTTTATTTTATCTTCGAG  
TACATGAAGGAAAATCTTTACCAGCTCATTAAAGAGAGAAAATAAGTTGTTTCCTGAGTCT  
GCTATAAGGAATATCATGTATCAGATATTACAAGGACTCGCATTTTATTCACAAACTCGGC  
TTCTTTTCATCGAGACTTAAAGCCTGAGAACCTCCTCTGCATGGGACCAGAACTTGTGAAA  
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TCTACCAGATGGTACAGGGCTCCAGAAGTACTCCTGAGGTCTACCAACTACAGCTCCCCC  
ATTGACGTCTGGGCGGTGGGCTGCATCATGGCAGAAGTTTACACCCTCAGGCCACTCTTC  
CCTGGAGCCAGTGAAATTGACACAATATTCAAAATTTGCCAAGTGCTGGGGACACCAAAA  
AAGACTGACTGGCCTGAAGGCTATCAACTTTCAAGTGCAATGAACTTCCGTTGGCCACAG  
TGTGTACCCAATAACTTAAAGACCTTGATTCCCAATGCTAGCAGTGAAGCAGTCCAGCTC  
CTGAGAGACATGCTTCAGTGGGATCCCAAGAAACGACCAACAGCTAGTCAGGCACTTCGA  
TATCCTTACTTCCAAGTTGGACACCCACTAGGCAGCACCCACACAAAACCTTCAGGATTCA  
GAAAAACCACAGAAAGGCATCCTGGAAAGGGCAGGCCCCACCTCCTTATATTAAGCCAGTC  
CCACCTGCCCCAGCCACCAGCCAAGCCACACACACGAATTTCTTCACGACAGCATCAAGCC  
AGCCAGCCCCCTCTGCATCTCACGTACCCCTACAAAGCAGAGGTCTCCAGGACAGATCAC  
CCAAGCCATCTCCAGGAGGACAAGCCAAGCCCGTTGCTTTTCCCATCCCTCCACAACAAG  
CATCCACAGTCGAAAATCACAGCTGGCCTGGAGCACAAAAATGGTGAGATAAAGCCAAAG  
AGTAGGAGAAGGTGGGGTCTTATTTCCAGGTCAACAAAGGATTTCAGATGATTGGGCTGAC  
TTGGATGACTTGGATTTTCAGTCCATCCCTCAGCAGGATTGACCTGAAAAACAAGAAAAGA  
CAGAGTGATGACACTCTCTGCAGGTTTGAGAGTGTTTTGGACCTGAAGCCCTCTGAGCCT  
GTGGGCACAGGAAACAGTGCCCCCACCAGACGTCATATCAGCGGCGAGACACGCCACC  
CTGAGATCTGCAGCCAAGCAGCACTATTTGAAGCACTCTCGATACTTGCCTGGGATCAGT  
ATAAGAAATGGCATACTCTCGAATCCAGGCAAGGAATTTATTCCACCTAATCCATGGTCT  
AGTTCTGGCTTGTCTGGAAAATCTTCAGGGACAATGTTCAGTAATCAGCAAAGTAAATTCA  
GTTGGTTCCAGCTCTACAAGTTCTAGTGGACTGACTGGAACTATGTCCCTTCCTTTCTG  
AAAAAGAAAATCGGTTCTGCTATGCAGAGGGTACACCTAGCACCTATTCCAGACCCCTTC  
CCTGGTTATTCTCTCCCTGAAGGCTCATGAGACCTCATCTGGGCGACCATTTCTTGGACACC  
CAGCCTAGAAGCACTCCTGGGTTGATACCAAGGCTCCAGCCGCCAGCCAGTGCATGGC  
CGGACAGACTGGGCTTCCAAGTACCCATCCCGGGCGGTGA



## FIGURE 2UU

SEQ ID NO: 59\_AA839940\_M

AGCAGCAACAATGGTGGCATGAGTGCAGAGGAGGAGATAGGGGCTGGGGCTGAGGCTATC  
AGAGGACCAAGCTTGGCTACAAGGGACTGGAGAGATGAGACTGTTGGGACCAAGAGCTC  
CAGCAAGGCATAGACCCAGGAGCAGTGAGCCCTGAGCCTGGGAAGGACCACGCAGCCCCAG  
GGCCCAGGAAGAACTGAAGCTGGAAGGGTATCTTCTGCTGCAGAGGCTGCCATTGTGGTT  
CTAGATGACAGCGCAGCACCCCCAGCCCCCTTTTGAACACCGGGTAGTGAGCATCAAAGAT  
ACCCTGATCTCAGCAGGCTACACGGTATCCCAACATGAAGTCTTAGGAGGGGGTCCGTTT  
GGCCAGGTGCACAGGTGTACAGAGAGGTCTACAGGCCTTGCACTGGCAGCCAAGATCATC  
AAAGTGAAGAACGTAAAGGACCGGGAGGATGTGAAGAATGAGGTCAACATCATGAACCAG  
CTCAGCCACGTAAACTTGATCCAACCTTTATGATGCGTTTGAGAGCAAGAACAGCTTCACT  
CTGATCATGGAGTATGTGGATGGAGGCGAACTCTTTGACCGGATCACGGATGAGAAGTAC  
CACCTCACTGAGTTGGATGTGGTCTTGTTTACGAGGCAGATCTGTGAGGGTGTGCATTAC  
CTGCATCAGCACTATATCCTGCACCTGGACCTCAAGCCTGAGAACATATTGTGTGTTCAGC  
CAGACAGGGCATCAAATTAAGATCATTGACTTTGGGCTGGCTAGAAGATACAAGCCTCGG  
GAGAAGCTAAAGGTGAACCTTTGGTACTCCGGAGTTCCTGGCCCCAGAAGTTGTAACTAT  
GAGTTTGTGTCAATTTCCAACAGACATGTGGAGTGTGGGAGTTATCACCTACATGCTACTC  
AGTGGTTTGTCCCCATTTCTAGGGGAGACAGATGCAGAGACCATGAATTTTATTGTGAAC  
TGCAGCTGGGATTTTCGATGCTGATACCTTCAAAGGGCTGTCCGAGGAAGCCAAGGACTTT  
GTTTCCCGGTTACTGGTCAAAGAGAAGAGCTGTAGGATGAGCGCCACACAGTGCCTGAAA  
CACGAGTGGTTAAATCACCTGCCTGCCAAAGCCTCGGGCTCCAACGTTCCGCTCAGATCC  
CAACAACCTGCTGCAGAAATATATGGCTCAGAGTAAATGGAAGAAACATTTCCACGTGGTG  
GCTGCAGTCAACAGGCTACGGAAATTTCCAACGTGTCCCTAATCTTCAACTCTGGTGTTT  
CACTGGGCTTGGGAATTTCTTGAGGCAACACGAAGTGGTAATATGAAGAGATTACTCAAGA  
TTTTATGTAGATTGGCGCTTTGCTATTATTGATTTTTCTTATTTTGCAAAGAATGATGGA  
AGGAAGCAAGAAAGAAAGAAAGAAAGAGGGGGAAGAAAGGAAAGGCAGAAAGCAA  
GGAAACAGGCTACGTTGTTGCTCTTCTTGTAGGTGAAAGTGTTTTTTATTAAAGCCCTAG  
GAATGTTTTTTCTGCCTCGTAAGGTCAGCAGGTCTCATATGCTGCTTGCTACCCCGCACCC  
TTCCTTTTGGTAATAAGAGCAGGCACGCTCAGGATGGGCAGGGAAATCCTACTTGGCTTT  
TGGTCAAATTTGAATTCTAACTTGTCTATGATTAAAGAAGCCAGTAGGGAGGGAGGTATG  
GAAGAGGGAGGAATTAGGTCCAACAGTGGGGGATGAATTTGACCGAAACATTGTATAAAA  
TTCTTAAAGAATTAATAAAATATATTTTAAAGGAG

SEQ ID NO: 60\_AA460132\_H

GGAACCTCAGGCTTCAGAGAGCCGAAAAGTTGGGAGGCGTAACCACTTACAGGCCGGAAG  
TGTCGGGGGTGGACGCATTCGGGTAGCCGAAGAAGTCCCAGGATTGCCGAAGAAGTCCCA  
GGATTTCCGAAGCGAGCCGAAGCATCGCGACAGTTTTTCAGAGACAGCTGATCGGTTGGAG  
CTGTTGCGCCGAGCAGTCATGGCGGCGGCCAGAGCTACTACGCCGGCCGATGGCGAGGAG  
CCCGCCCCGGAGGCTGAGGCTCTGGCCGCAGCCCGGGAGCGGAGCAGCCGCTTCTTGAGC  
GGCCTGGAGCTGGTGAAGCAGGGTGCCGAGGCGCGCGTGTTCGTTGGCCGCTTCCAGGGC  
CGCGCGGCGGTGATCAAGCACCGCTTCCCCAAGGGCTACCGGCACCCGGCGCTGGAGGCG  
CGGCTTGGCAGACGGCGGACGGTGCAGGAGGCCCCGGGCGCTCCTCCGCTGTGCGCGCGCT  
GGAATATCTGCCCCAGTTGTCTTTTTTTGTGGACTATGCTTCCAACCTGCTTATATATGGAA  
GAAATTGAAGGCTCAGTGAAGTGTTCGAGATTATATTCAGTCCACTATGGAGACTGAAAAA  
ACTCCCCAGGGTCTCTCCAACCTTAGCCAAGACAATTGGGCAGGTTTTTGGCTCGAATGCAC  
GATGAAGACCTCATTTCATGGTGATCTCACCACTCCAACATGCTCCTGAAACCCCCCTG  
GAACAGCTGAACATTGTGCTCATAGACTTTGGGCTGAGTTTCATTTTCAGCACTTCCAGAG  
GATAAGGGAGTAGACCTCTATGTCCTGGAGAAGGCCTTCCCTCAGTACCCATCCCAACACT  
GAAACTGTGTTTGAAGCCTTTCTGAAGAGCTACTCCACCTCCTCCAAAAAGGCCAGGCCA  
GTGCTAAAAAAATTAGATGAAGTGCGCCTGAGAGGAAGAAAGAGGTCCATGSTTGGGTAG  
AAGAATGTGTATGACAACCACACACAGTGAAGCTCTTTTTTCAAAGTAAATTTGAAGAAA

## FIGURE 2VV

TGCTACAAGTATGAGATGAGATCTAAGTAAAGGTGTTAAGATATTTTTTAAGTGGTATGTC  
ATCGTSTCATTATCATCTGCACTTCACTCAAGAGCTTACTATGTGTCTAAGTCATSTTCT  
AGGCAGAATTGGGTATTTAAAGTAAATTGAGGACAGGCTTCTCCCAGATTGTGACATGTA  
TATCTCAGATACATGGGTGTGGCATTGAACACATAATGAGAACATTATTCTCTTTTATG  
TCCTTGTGAGACAAGGATGAAGTCTCAGTTGCTGATACTCGCTGAGCTTACTGGCCCTCT  
AACCCAGTGTTTTTTTTTTGTTGTTGTTGTTGTGTACATGTTATATTTATTTTGAAACCAGTTT  
AATGGGATACAACCAGCATTTTAAAAAATGAAATAGAATACAGCATGG

SEQ ID NO: 61\_SGK034\_H

CAGAGAGAGAAGGTAAACCAAGGGAACATGCCAGGGCTTCAGAGCACCTTCCTAGCCATG  
GACACGGAGGAGGGGGTAGAGGTGGTGTGGAACGAGCTCCACTTCGGAGACAGGAAGGCC  
TTCGCGGCGCACGAGGAGAAGATCCAGACCGTGTTTCGAGCAGCTGGTGCTGGTGGACCAC  
CCGAACATCGTGAAGTTGCACAAGTACTGGCTGGATACCTCTGAGGCCTGCGCGAGGGTC  
ATCTTCATCACAGAGTACGTGTCATCAGGCAGCCTCAAGCAATTCCTCAAAAAGACCAAG  
AAGAACCACAAGGCCATGAACGCCCCGGGCCTGGAAGCGCTGGTGCACGCAGATCCTGTCT  
GCGCTCAGCTTCCTGCACGCCTGCAGCCCCCAATCATCCACGGGAACCTGACCAGCGAC  
ACCATCTTCATTCAGCACACGGCCTCATCAAGATCGGCTCCGTGTGGCACCGAATCTTC  
TCCAATGCACTTCCAGATGATCTCCGAAGCCCCATCCGCGCTGAGCGAGAGGAACTTCGG  
AACCTGCACTTCTTCCCCCAGAGTATGGAGAGGTGGCCGATGGGACCGCTGTGGACATC  
TTCTCCTTTGGGATGTGTGCGCTGGAGATGGCTGTACTGGAAATCCAGACCAATGGGGAC  
ACCCGGGTACAGAGGAGGCCATTGCTCGCGCCAGGCACTCGCTGAGTGACCCCAACATG  
CGGGAGTTCATCCTTTGCTGCCTGGCCCCGGGACCCTGCCCCGCGGCCCTCTGCCCCACAGC  
CTCCTCTTCCACCGCGTGCTCTTCGAGGTGCACTCGCTGAAGCTCCTGGCAGCCCACTGC  
TTCATCCAGCACCAAGTACCTCATGCCTGAGAATGTGGTGGAGGAGAAGACCAAGGCCATG  
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TACCCACTGATGAACCTTTGCAGCCACTCGACCCCTGGGGCTGCCCCGTGTGCTGGCCCCA  
CCCCCGGAGGAGGTCCAAAAGGCCAAGACCCCGACGCCAGAGCCCTTTGACTCTGAGACC  
AGAAAGGTCATCCAGATGCAGTGCAACCTGGAGAGAAGCGAGGACAAGGCGCGCTGGCAT  
CTCACTCTGCTTCTGGTGTGGAAGACCGGCTGCACCGGCAGCTGACCTACGACCTGCTC  
CCAACGGACAGCGCCCAGGACCTCGCCTCGGAGCTCGTGCACTATGGCTTCCTCCACGAG  
GACGACCGGATGAAGCTGGCCGCCTTCCTGGAGAGCACCTTCCTCAAGTACCGTGGGACC  
CAGGCCTGACCCGGAGCCCCAGCCCCAGGGGACCATGCCGGGGTGCTGCCCGGGCAGGCC  
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GCCCCGGTAGTGAAGGAACCCCCCGTCTCCTGAGAGTGGGGCTGACCCTGCCTTGGGCGC  
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GCCTGGCTGGGGCCACTGCCTCCTCAGCATGCAGGAGGCTGCCCTGTAGGGAACCCACAGC  
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GGTCCCACACAGCTCTGCCCTAGAGCCACCTCTTTGACCCTTTACCCACCCTGAGACCAG  
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TCACAGCCCCCTCCATGTTACCTCCCGCACCTCCTCCCTGGGGCAGCTGCTCCCTGGGCCT  
CTGAGGATGTCAGCTCCTGGCTCCCTGCCTCTCTCCCACTCCACTCCTGGCTCAGTCTTA  
GAGATTTCTATGCCCTCATGGATTCTACCCCTGCCTTCCTGGCCTCTTGATTCTTGGCTT  
GCCTCTCCTCCAATTCCAACTTAGTGAAATGGCCTTAAGCATTTTAAACTGTATGTATA  
CATTAGCGCATTCATGCCTTTCTAAACGCATTTCAAATGTCAACCAGGAAGGCACACCAC

## FIGURE 2WW

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CTGCTGGCAGAATCCACATCCTTTTCGGTGGCAGGGGCCAAGGTCCCCACTTTCTTGCTGAC  
TGTAAGCTAAGGCCACTTCCAGCTTGTAGAGGCTGCCTACATTCCTTGGCTCTTGGCCCC  
CTCCTCCATCTTCAGAGCTAGCAGGTTCACTCTGTGTACGAACCATTTCTCTGGTTCCCT  
TGCAGACAGGAAAGGTTGTCCCTAAGGACTCATGAGATTAGGTTGGGGCCAGCCAGATAA  
TACATGATAATCTCCCTCCTCAAGGTTTTTAATATTAAACACATCTGCAGGACACATTTT  
GCCATGTAACTAACATTCACTGGTTCCAGGGATTAAGGAATGAACCTCTTTTGTGTTGGGG  
AAGGGTGGCATTCTGCTGACCACAGCACTCCAACCAAAGGCCAAAACCAAAGCAAGACT  
TACTAACGCATATCAAATAAATTAAAGGTACAAAATCGTGAATCTCAGTTATCTTAAATA  
TTCCAATACTATTTACAAAATTATTCAAATTCTCACGCCTTCCAACCTCAAATTAGCAAT  
CTAAAGTAATTTCCATATCCTAGATGGAAACCCTCATGCTAAACTGTCTGATTATGCATG  
GTTCTAAATGGTTTCAGTGGCAAATACATAACATTGTACTACTGATTAAACTGAACTTAA  
AAGC

SEQ ID NO: 62\_AA103218\_M SGK034\_M

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CTCCTTCGGGATGTGTGCACTGGAGATGGCTGTACTCGAGATCCAAGCCAACGGGGATAC  
CAGAGTCACAGAAGAGGCCATCGCTCGAGCCAGGCACTCACTGAGTGACCCCAACATGCG  
GGAATTCATCCTCTCCTGCCTGGCCCCGGGACCCTGCCCGCCGACCCTCAGCCCACAACCT  
CCTCTTCCACCGAGTGCTCTTTGAGGTGCACTCGCTGAAGCTGCTGGCAGCTCACTGCTT  
CATCCAGCACCAGTACCTCATGCCTGAGAATGTGGTAGAGGAAAAGACCAAGGCCATGGA  
CCTCCATGCAGTTTTTGGCTGAGATGCCGCAGCCCCATGGACCCCCAATGCAGTGGCGGTA  
CTCAGAGGTCTCCTTCTTGGAGCTGGACAAATTCCTAGAGGATGTCAGGAACGGGATCTA  
TCCACTGATGAACTTTGCGGCTGCTCGGCCCTTGGGGCTTCCCCGTGTGTTGGCCCCACC  
CCCAGAGGAAGCCCCAAAAGGCCAAAACCTCCAACGCCAGAACCCTTTGACTCGGAGACCAG  
GAAGGTGGTCCAGATGCAGTGCAACCTGGAAAGAAGCGAGGACAAGGCTCGGTGGCACCT  
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AACGGACAGTGCCCAGGACCTCGCTGCTGAACTAGTGCATTATGGCTTCCTGCACGAGGA  
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AGCGTGACCTTCCCAGTCCTGACGGCCCAGCAGAGATACAGGGGCTCAGGGTTGTCCACT  
TGGCAAAGAGCCCCCACACTGCTCAAAGCTGCCTTCTGCCTGTGTTCCCTGGAACCTGAAC  
ACAGGCCCTGCTAGTGAAGACACCCCCACCCCCCAGCTTTCTGCAGCAGTGTGGGACCCT  
GGGGTGGTGATGGAGCCCTGAGCCTGGACGAGAGTGGATACAGGTCAAGTTAGGGGAACCG  
CTCCATCTGGTACTAGACAACAGCCATGCCTTCAGGTGGCATAGAAACCTAGGGAAGGAG  
CCTGAACTCAGGTGTCACAGTGCTGGGCATCAGGCAGACCAGACCTGACCTGATTGGAGA  
ACTGTAGACTAGATAGCTTGGAGTTGAACCCATGGCCAGGGAATTCCTTGGTCCTGCTCA  
GACCAGTCCTGATCCCTTGCAGACCTGCCTTGAGCCCTCTTTCTGATCTTCCACACTCTT  
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TCTGGCCTAGGGGCTCAGGGGTCAGGCATCCTCCACATTCCCTCCCTGGGGAAGTTGTGT  
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TCTTACTGGTTTCAAAGTCCTGATGAACGCTTCCCCTCAGAGCCACCCTGGTTTCCTTGG  
TTCTTGAAGTGCCTCTCTCCCAACTTCAAACCAGGTCTTAAACGTTTTTTTAAATGCATAT  
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TTTGAGACGACACACACACACACACACACACACAGAGAGAGAGAGAGTCTGTA  
CATCAAGTGTGATCCAGGCTCTCACTAGATTAATACCCAGGCTAAGTTCCTTTCTGGAAG  
CTGGGACTTACCTCCTGCTCCTTCAAGCTATTGGCAGAACTCACTTCCCTGCAATGGTAA  
GGCAGAAATCCCTATTTTCTCAACAGCTGCCAACTAAGAACCCTCTCAGCTTCTAGAGG

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## FIGURE 2XX

CCACCAACTTTTCTTAGTTCTTCTTTCTCCCCCTCAAGACCAGCAGCGTCAAGTTGAAT  
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CACACCTGCGCAGTTCTTCTGCTGTCATCCTGGGCTTTGGTGCTTGGAGAACAGCCGTG  
GGCGGTGGGTGTTGTTACTGTGGTACCTACCATGCCATCTTAACCGAAACCAAGACCTAA  
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SEQ ID NO: 63\_NEK7\_H, N34132\_H

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TGACCGGCAGGACCGAGGAGTACAGGCGCCGCGCCACACTATGGACAAGGACAGCCGTG  
GGGCGGCGCGACCACTACCACCACTGAGCACCGCTTCTTCCGCGGAGCGTCATCTGCG  
ACTCCAATGCCACTGCACTGGAGCTTCCCGGCCTTCTTCTTTCCCTGCCCCAGCCCAGCA  
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GCGGCAGCGCCAAGGAGCCACAGGAGGAACGGAGCCAGCAGCAGGATGATATCGAAGAGC  
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TCGGCAGAGGCTCCTTTAAGACGGTCTACAAAGGTCTGGCACTGAAACCACCGTGGAAG  
TCGCCTGGTGTGAACTGCAGGATCGAAAATTAACAAAGTCTGAGAGGCAGAGATTTAAAG  
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GAACACTTAAAACGTATCTGAAAAGGTTTAAAGTGATGAAGATCAAAGTTCTAAGAAGCT  
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GAGACCTCGGTCTGGCAACCCTGAAGCGGGCTTCTTTTGCCAAGAGTGTGATAGGTACCC  
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GCAGTCTCAAACAGCAGGTAGAACAATCCAGTGCTTCCCAGACAGGAATCAAGCAGCTCC  
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AGCCGACCACTTTGGCTTCTCTGTAGACAGTGACATTCAGATGTTGCTTCAGGTATGA  
GTGATGGCAATGAGAACGTCCCATCTTCCAGTGGAAGGCATGAAGGAAGAACTACAAAAC



## FIGURE 2YY

GGCATTACCGAAAATCTGTAAGGAGTCGCTCTCGACATGAAAAAACTTCACGCCCAAAT  
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## FIGURE 2ZZ

CTTTGTATACCAAACCTGGGCAAGGTGCCCCCTGCTGTTATTATTCCCCCAGCTGCTCCCC  
TTTCAGGGAGAAGACGACGACCCACTAAAAGCAAAGGCAGCAAATCTAGTCGAAGCAGTT  
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GTGAAAAGGGGAAGTGAGTGATAATGAGAATCGGTGGGCTCACTGCTCCCATTAGGTGAA  
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CCATCTCT

SEQ ID NO: 64\_BCON3\_H

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CCTGGCCATGGATACAGAGGAAGGTGTAGAGGTTGTGTGGAATGAGGTACAGTTCTCTGA  
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GACCTGTGACACCATCTTCATCCAGCACACGGACTCATCAAGATTGGCTCTGTGGCTCC  
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TGCCGTACTGGCTGAAATCCCTGCAGGACCAGGAAGAGAACCAGTTTCAGACTTTGTACTC  
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GGTGGTGCTGATGCAGTGCAACATTGAGTCGGTGGAGGAGGGAGTCAAACACCACCTGAC  
ACTTCTGCTGAAGTTGGAGGACAAACTGAACCGGCACCTGAGCTGTGACCTGATGCCAAA  
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GAAGTGAGACACGAAAGGTGGTGCTGATGCAGTGCAACATCGAATCTGTGGAGGAGGGA  
GTCAAACACCATCTAACACTTCTGCTGAAGCTGGAGGACAAATTGAACCGGCACCTGAGC  
TGTGACCTGATGCCAAATGAGAGCATCCCGGACTTGGCAGCTGAGCTGGTGCAGCTGGGC  
TTCATTAGTGAGGCTGATCAGAGCCGCCTGACTTCTCTGCTGGAGGAGACGCTCAACAAG  
TTCAACTTCACCAGGAACAGTACACTCAACACAGCCACTGTACCCGTCTCCTCGTAGAGC  
TCACTTGAGCCAGGCCCTAGCCAGGCTGTGGCTGTCCCTGGGCATGCTGCAGTCCCTCT  
GTCCCTTCTCCCCAGTCAGTATTACCCTTCGCGCCCATATTATTTAGGAGGGCTTTAGGG  
GCTCCCTGGTTGAGTATCACCTTGCCCCCTTCCCCTCTCTTCCCTCCCCCTCTGCACTTTGTT  
TACTTGTTTTTGCACAGACGTGGGCCTGGGCCTTCTCAGCAGCCACCTTCTAGCTGGGGGC  
TAGTAGCTGACCTGCTGCCTCCTGCCCTACTTGTGTGGACAGGAGGCCCCACGGGCACTGG  
GGAAGCTGAGTTCTACAATCCCGCTGGGGCGCATGGGCAGGAGAGAAAGGTGGTGCTGCA  
GGGGTGGCCCCCGGGGGGGGCATTGGAATCACCTCAGTTGCTGCTGTAATAAAGTCTAC  
TTTTTGCT



## FIGURE 2BBB

SEQ ID NO: 66\_AA099102\_H

ATGTCATCATGTGTCTCTAGCCAGCCCAGCAGCAACCGGGCCCGCCCCCAGGATGAGCTG  
GGGGGCAGGGGCAGCAGCAGCAGCGAAAGCCAGAAGCCCTGTGAGGGCCCTGCGGGGGCTC  
TCATCCTTGAGCATCCACCTGGGCATGGAGTCCTTCATTGTGCTCACCGAGTGTGAGCCG  
GGCTGTGCTGTGGACCTCGGCTTGGCGCGGGACCGGCCCTGGAGGGCCGATGGCCAAAGAG  
GTCCCCCTTGACACCTCCGGGTCCCAGGGCCCGGCCCCACCTCTCCGGTCGCAAGCTGTCT  
CTGCAAGAGCGGTCCCAGGGTGGGCTGGCAGCCGGTGGCAGCCTGGACATGAACGGACCG  
TGCATCTGCCCCGTCCCTGCCCTACTCACCCGTGAGCTCCCCGAGTCCTCGCCTCGGCTG  
CCCCGGCGGGCCGACAGTGGAGTCTCACCACGTCTCCATCACGGGTATGCAGGACTGTGTG  
CAGCTGAATCAGTATAACCCTGAAGGATGAAATTGGAAAGGGCTCCTATGGTGTGTCGTCAG  
TTGGCCTACAATGAAAATGACAATACCTACTATGCAATGAAGGTGCTGTCCAAAAAGAAG  
CTGATCCGGCAGGCCGCTTTTCCACGTGCCCCCTCCACCCCGAGGCACCCGGCCAGCTCCT  
GGAGGCTGCATCCAGCCCAGGGGCCCCATTGAGCAGGTGTACCAGGAAATTGCCATCCTC  
AAGAAGCTGGACCACCCCAATGTGGTGAAGCTGGTGGAGGTCCTGGATGACCCCAATGAG  
GACCATCTGTACATGGTGTTCGAACTGGTCAACCAAGGGCCCGTGATGGAAGTGCCCAAC  
CTCAAACCACTCTCTGAAGACCAGGCCCGTTTCTACTTCCAGGATCTGATCAAAGGCATC  
GAGTACTTACACTACCAGAAGATCATCCACCGTGACATCAAACCTTCCAACCTCCTGGTC  
GGAGAAGATGGGCACATCAAGATCGCTGACTTTGGTGTGAGCAATGAATTCAAGGGCAGT  
GACGCGCTCCTCTCCAACCTACGTGGGCACGCCCCGCTTCATGGCTCCCGAGTCGCTCTCT  
GAGACCCGCAAGATCTTCTCTGGGAAGGCCAAGGATGTTTGGGGCCATGGGTGTGACACTA  
TACTGCTTTGTCTTTGGCCAGTGCCCATTCATGGACGAGCGGATCATGTGTTTACACAGT  
AAGATCAAGAGTCAGGCCCTGGAATTTCCAGACCAGCCCGACATAGCTGAGGACTTGAAG  
GACCTGATCACCCGTATGCTGGACAAGAACCCCGAGTCGAGGATCGTGGTGCCGGAAATC  
AAGCTGCACCCCTGGGTACGAGGCATGGGGCGGAGCCGTTGCCGTGCGAGGATGAGAAC  
TGCACGCTGGTTCGAAGTGACTGAAGAGGAGGTCGAGAACTCAGTCAAACACATTCCCAGC  
TTGGCAACCGTGATCCTGGTGAAGACCATGATACGTAAACGCTCCTTTGGGAACCCATTC  
GAGGGCAGCCGGCGGGAGGAACGCTCACTGTCAGCGCCTGGAACTTGCTCACCAAAAAA  
CCAACCAGGGAATGTGAGTCCCTGTCTGAGCTCAAGGAAGCAAGGCAGCGAAGACAACCT  
CCAGGGCACCGACCCGCCCCCGGTGGGGGAGGAGGAAGTGCTCTTGTGAGAGGCAGTCC  
TGCGTGGAAGTTGCTGGGCCCCCGCCCCCGGCTCCCCCGCACGCATGCATCCACTGCGG  
CCGGAGGAGGCCATGGAGCCCGAGTAG

SEQ ID NO: 67\_5R69\_17\_2\_H

CCGGGATGTGAGCCTGGTGGTTGGCAGCTGGAGCCACGTCGGAGGGGGGAAGTGTGCGAGC  
ATTCTCTGCAGGCATCACAGACCTGAGGCAGTGGCCTCCGGAGGGGCACTGGACAGAAACA  
GCCATCCAAGTGGCTGAGTGGAGGGACCCTGCTCAAGTGCAGCTGCAGTGGCCGGGGTTT  
CCCTCAGGTAGGGATCGGGGCGCCTTGTCGCCGCCAGCCACGTGTGGCGTCCGGTACAGT  
CAGCAGAGTGCAGGGTGCGGGCACCAGGAAAGGGGGCGCAGGGGGAACCTCCCGCGGGCCTC  
GCGTTTGCAAACCTTCTCGCCTGGGCAGGAGGCGGTGCTGGGAAAGAAGGTGGAAGAGCGA  
GCTTTTTTGGAACCTGTGCACGGGACAGATTGGACGCACACCCCTCGGGAGGCGCGAAGGCA  
TGGAAAATTTGAAGCATATTATCACCCCTTGGCCAGGTCATCCACAAACGGTGTGAAGAGA  
TGAAATACTGCAAGAAACAGTGCCGGCGCCTGGGCCACCGCGTCCTCGGCCTGATCAAGC  
CTCTGGAGATGCTCCAGGACCAAGGAAAGAGGAGCGTGCCCTCTGAGAAGTTAACCACAG  
CCATGAACCGCTTCAAGGCTGCCCTGGAGGAGGCTAATGGGGAGATAGAAAAGTTTCAGCA  
ATAGATCCAATATCTGCAGGTTTCTAACAGCAAGCCAGGACAAAATACTCTTCAAGGACG  
TGAACAGGAAGCTGAGTGATGTCTGGAAGGAGCTCTCGCTGTTACTTCAGGTTGAGCAAC  
GCATGCCTGTTTACCCATAAGCCAAGGAGCGTCCTGGGCACAGGAAGATCAGCAGGATG  
CAGACGAAGACAGGCGAGCTTTCCAGATGCTAAGAAGAGATAATGAAAAAATAGAAGCTT  
CACTGAGACGATTAGAAATCAACATGAAAGAAATCAAGGAAACTTTGAGGCAGTGTAAGT  
TATCATGTGCCCTGCTGTTTCTGATGGCCCCCAAACCTAGAAGTCATCAGTTTACTGGGAC



## FIGURE 2CCC

CCCAGCCTCCCGCTACCCCTGCATTTGTCCATTTTCTGTGCTGGATGGCTGGAAGCAGCC  
CACAGGTTTGGGGATCCATTCATGGCTAGCCCAGGCTTCTGTCCATGGAATAACATGTGG  
AGAGAGCTTCTTGACCAGTAAGATACCTTCTAGCAGCTGTCAAAGTACTTAAAAACCTCT  
ATGAATAGAATCAAAGCTTCAGTTCAGTTGCTGAATTTCCAAGAAGAAATTCAAATCAAA  
TTTAAATGCCCCACTCATTTCATTCAACAAAACCTGTGAGTATCTGGTTTATGCCAGA  
GGCCATGCAAAGAGGTAAGATGCAGAGAAGGACACTGCCTTCCAGGAGCTCACGGG  
GTGGAGGAGGAAAGAGGAAAGACAGACAGTGAACACACAACAGCAAGGTTACTGAGCTTG  
AACTATGTCCCTAACTACTAGATCTGAAATGACTACGCCAGATGCCAGATGCTCAAGTGC  
CAAGCTCTGGGTAACAGGAATAGACATCCTTCCAGGATGAGAGAGATGAGTCTGGATGAG  
GGTTAAGGCTGGAGGGACAGGCGGGATTTGAAGAGGAGGGAAAGGAAGTGGATGACACAT  
TCTGTAACTGTCCAGCTGTGTCTCTACTGGTCACTCAGAGGCACGGGAGCCGCTCCCTT  
GGGCTGAGTCCATCAGAAGCCCCAGCCACCACCAGCTCTGGTTCATGTAGTAGAGCTTCC  
CACTCACACATCACAAATATGCCACCTCCCTTAGGACCCCTTCTCTGCTCATTGACTCT  
TTTGTCTTCTTCTCTCGGGGGTGAGGTCAGATTTACCACCAAATGCATGCAGGAGAT  
CCCGCAAGAGCAAATCAAGGAGATCAAGAAGGAGCAGCTTTCAGGATCCCCGTGGATTCT  
GCTAAGGGAAAATGAAGTCAGCACACTTTATAAAGGAGAATACCACAGAGCTCCAGTGGC  
CATAAAAGTATTCAAAAACTCCAGGCTGGCAGCATTGCAATAGTGAGGCAGACTTTCAA  
TAAGGAGATCAAAACCATGAAGAAATTCGAATCTCCCAACATCCTGCGTATATTTGGGAT  
TTGCATTGATGAAACAGTGACTCCGCCTCAATTCTCCATTGTCATGGAGTACTGTGAAC  
CGGGACCCTGAGGGAGCTGTTGGATAGGGAAAAAGACCTCACACTTGGCAAGCGCATGGT  
CCTAGTCCTGGGGGCAGCCCGAGGCCTATACCGGCTACACCATTGAGAAGCACCTGAACT  
CCACGGAAAAATCAGAAGCTCAAACCTCCTGGTAACTCAAGGCTACCAAGTGAAGCTTGC  
AGGATTTGAGTTGAGGAAAACACAGACTTCCATGAGTTTGGGAACTACGAGAGAAAAGAC  
AGACAGAGTCAAATCTACAGCATATCTCTCACCTCAGGAACTGGAAGATGTATTTTATCA  
ATATGATGTAAAGTCTGAAATATACAGCTTTGGAATCGTCCTCTGGGAAATCGCCACTGG  
AGATATCCCGTTTCAAGGTGAAGAATGTGAAGACTGGCTCAGCCAGTGGCTGTAATTCTG  
AGAAGATCCGCAAGCTGGTGGCTGTGAAGCGGCAGCAGGAGCCACTGGGTGAAGACTGCC  
CTTCAGAGCTGCGGGAGATCATTGATGAGTGCCGGGGCCCATGATCCCTCTGTGCGGCCCT  
CTGTGGATGAAATCTTAAAGAACTCTCCACCTTTTCTAAGTAGTGTATCAAAATCTAAA  
CCAAGGAGTCTCTGGACAAGAAGCTGGGAGAGGCACGAACTGGACATCTCTCTCTCAT  
ATCCTTCGGCATTGGGTATCTATGGGTGCAAGGAGTGGGCACGCTTCTCTGTTACAAAT  
AGAAAACGATTCCAGTCATACAGGACACATCCCCTCCAAATGATATTTCCAAAAACATA  
CCTCTGACAGTAACTTTGATAGATGGTTTGTCAAATGTATCTTTCTGGGTATCCACACCT  
CTTGGCAATGAAATTTGCAGCTCCTCCCTTCCATAAATGAAGTCTCTTTCCCCACCATT  
GAATCTGGGCTGGCACTGTGACTTGATTTGATCAATAGAATGTGGAAGAAGTGAAGTGTAT  
GCCAGTTCCAAGCCTAGGTTTCAAGAGGCCTTATAAATGTCTGTTGGAACCTTACCCAGC  
CATGGACATGTTGAGTGAGCATGCTGGAGAATGAGAGACCACATGAAGCAGAAACATGCT  
TTCCTAGCTGAAGTCATACTAGCCCAACCAACATGGCAGCTAACACATGAATGAGGCCAA  
TCAAGACCAGAAGAACCCTCAAGCAGATCCCAGCCCAAATTGCCCATTCACACAATCAG  
GAGCTAAATAAATTACTGTTGTCTTTT

SEQ ID NO: 68\_H85811\_H

CGCCCGGCCCCCTCCCCCGGCGCCGGCCACGGGAGGCGGTGATGCGGGCGCGGGCGGCCT  
CGGCTGCGCCGAGAGCGGAGACACAGGCTCAAGATGGCAGATTCCGACTGAGGCTGGGGG  
GGCCGAGCTCGCGCGCCGCTTTCCCGTCCCCGTGCCATGAACCGCGGACACCCCGGCCC  
CGATGGCCCCCGTGTACGAAGGTATGGCCTCACATGTGCAAGTTTTCTCCCTCACACCC  
TTCAATCAAGTGCCTTCTGTAGTGTGAAGAACTGAAAATAGAGCCGAGTTCCAAGTGGG  
ACATGACTGGGTACGGCTCCCACAGCAAAGTGTATAGCCAGAGCAAGAACATCCCCCTGT  
CGCAGCCAGCCACCACAACCGTCAGCACCTCCTTGCCGGTCCCAAACCCAAGCCTACCTT  
ACGAGCAGACCATCGTCTTCCCAGGAAGCACCGGGCACATCGTGGTCACCTCAGCAAGCA

## FIGURE 2DDD

GCACCTTCTGTCACCGGGCAAGTCCCTCGGGGGACACACAACCTAATGGGTGGAAGCACTG  
TGAGCCTCCTTGATACCTACCAAAAATGTGGACTCAAGCGTAAGAGCGAGGAGATCGAGA  
ACACAAGCAGCGTGCAGATCATCGAGGAGCATCCACCCATGATTCAGAATAATGCAAGCG  
GGGCCACTGTGCGCCACTGCCACCACGTCTACTGCCACCTCCAAAAACAGCGGCTCCAAACA  
GCGAGGGCGACTATCAGCTGGTGCAGCATGAGGTACTGTGCTCCATGACCAACACCTACG  
AGGTCTTAGAGTTCTTGGGGCCGAGGGACGTTTGGGGCAAGTGGTCAAGTGCTGGAAACGGG  
GCACCAATGAGATCGTAGCCATCAAGATCCTGAAGAACCACCCATCCTATGCCCGACAAG  
GTCAGATTGAAGTGAGCATCCTGGCCCCGGTTGAGCACGGAGAGTGCCGATGACTATAACT  
TCGTCCGGGGCCTACGAATGCTTCCAGCACAAGAACCACACAGTGCTTGGTCTTCGAGATGT  
TGGAGCAGAACCTCTATGACTTTCTGAAGCAAAACAAGTTTAGCCCCCTTGCCCCCTCAAAT  
ACATTTCGCCCAGTTCTCCAGCAGGTAGCCACAGCCCTGATGAAACTCAAAGCCTAGGTC  
TTATCCACGCTGACCTCAAACCAGAGAACATCATGCTGGTGGATCCATCTAGACAACCAT  
ACAGAGTCAAGGTCATCGACTTTGGTTTCAGCCAGCCACGTCTCCAAGGCTGTGTGCTCCA  
CCTACTTGCAGTCCAGATATTACAGGGCCCCCTGAGATCATCCTTGGTTTACCATTTTGTG  
AGGCAATTGACATGTGGTCCCTGGGCTGTGTTATTGCAGAATTGTTCCCTGGGTTGGCCGT  
TATATCCAGGAGATTTCGGAGTATGATCAGATTTCGGTATATTTTCACAAACACAGGGTTTGC  
CTGCTGAATATTTATTAAGCGCCGGGACAAAGACAACCTAGGTTTTTCAACCGTGACACGG  
ACTCACCATATCCTTTGTGGAGACTGAAGACACCAGATGACCATGAAGCAGAGACAGGGA  
TTAAGTCAAAAGAAGCAAGAAAGTACATTTTCAACTGTTTAGATGATATGGCCCAGGTGA  
ACATGACGACAGATTTGGAAGGGAGCGACATGTTGGTAGAAAAGGCTGACCGGCGGGAGT  
TCATTGACCTGTTGAAGAAGATGCTGACCATTGATGCTGACAAGAGAATCACTCCAATCG  
AAACCCTGAACCATCCCTTTGTCAACCATGACACACTTACTCGATTTTCCCCACAGCACAC  
ACGTCAAATCATGTTTCCAGAACATGGAGATCTGCAAGCGTCGGGTGAATATGTATGACA  
CGGTGAACCAGAGCAAAACCCCTTTCATCACGCACGTGGCCCCCAGCACGTCCACCAACC  
TGACCATGACCTTTAACAACCAGCTGACCACTGTCCACAACCAGCCCTCAGCGGCATCCA  
TGGCTGCAGTGGCCCAGCGGAGCATGCCCTGCAGACAGGAACAGCCCAGATTTGTGCCC  
GGCCTGACCCGTTCCAGCAAGCTCTCATCGTGTGTCCCCCGGCTTCCAAGGCTTGCAGG  
CCTCTCCCTCTAAGCACGCTGGCTACTCGGTGCGAATGGAAAATGCAGTTCCCATCGTCA  
CTCAAGCCCCAGGAGCTCAGCCTCTTCAGATCCAACCAGGTCTGCTTGCCCAGCAGGCTT  
GGCCAAGTGGGACCCAGCAGATCCTGCTTCCCCCAGCATGGCAGCAACTGACTGGAGTGG  
CCACCCACACCTCAGTGCAGCATGCCACCGTGATTCCCGAGACCATGGCAGGCACCCAGC  
AGCTGGCGGACTGGAGAAATACGCATGCTCACGGAAGCCATTATAATCCCATCATGCAGC  
AGCCTGCACTATTGACCGGTCTATGTGACCCTTCCAGCAGCACAGCCCTTAAATGTGGGTG  
TGGCCCACGTGATGCGGCAGCAGCCAACCAGCACCCACCTCCTCCCGGAAGAGTAAGCAGC  
ACCAGTCATCTGTGAGAAATGTCTCCACCTGTGAGGTGTCTCCTCTCAGGCCATCAGCT  
CCCCACAGCGATCCAAGCGTGTCAAGGAGAACACACCTCCCCGCTGTGCCATGGTGCACA  
GTAGCCCCGGCCTGCAGCACCTCGGTACCTGTGGGTGGGGCGACGTGGCCTCCAGCACCA  
CCCGGGAACGGCAGCGGCAGACAATTGTCATTCCCGACACTCCAGCCCCACGGTCAGCG  
TCATCACCATCAGCAGTGACACGGACGAGGAGGAGGAACAGAAACACGCCCCCACCAGCA  
CTGTCTCCAAGCAAAGAAAAACGTCTATCAGCTGTGTACAGTCCACGACTCCCCCTACT  
CCGACTCCTCCAGCAACACCAGCCCCCTACTCCGTGCAGCAGCGTGCTGGGCACAACAATG  
CCAATGCCTTTGACACCAAGGGGAGCCTGGAGAATCACTGCACGGGGAACCCCCGAACCA  
TCATCGTGCCACCCCTGAAAACCCAGGCCAGCGAAGTATTGGTGGAGTGTGATAGCCTGG  
TGCCAGTCAACACCAGTCACCACTCGTCCTCCTACAAGTCCAAGTCCTCCAGCAACGTGA  
CCTCCACACAGCGGTCACTCTTCAGGGAGCTCATCTGGAGCCATCACCTACCGGCAGCAGC  
GGCCGGGGCCCCCACTTCCAGCAGCAGCAGCCTCAATCTCAGCCAGGCTCAGCAGCACA  
TCACCACGGACCGCACTGGGAGCCACCGAAGGCAGCAGGCTACATCACTCCACCATGG  
CCCAGGCTCCGTACTCCTTCCCGCACAAACAGCCCCAGCCACGGCACTGTGCACCCCGCATC  
TGGCTGCAGCCGCTGCGGCTGCCACCTCCCCACCCAGCCCCACCTCTACACCTACACTG  
CGCCGGCGGGCCCTGGGCTCCACCGGCACCGTGGCCCACTGGTGGCCTCGCAAGGCTCTG

## FIGURE 2EEE

CGCGCCACACCGTGCAGCACACTGCCTACCCAGCCAGCATCGTCCACCAGGTCCCCGTGA  
GCATGGGCCCCCGGGTCCTGCCCTCGCCCACCATCCACCCGAGTCAGTATCCAGCCCAAT  
TTGCCCCACCAGACCTACATCAGCGCCTCGCCAGCCTCCACCGTCTACACTGGATACCCAC  
TGAGCCCCGCCAAGGTCAACCAGTACCCTTACATATAAACACTGGAGGGGGAGGGAGGGAG  
GGAGGGAGGGAGAGAAATGGCCCCGAGGGAGGGAGGGAGAGAAAGGAGGGAGGGCGCTCCTGGGA  
CCGTGGGCGCTGGCCTTTTATACTGAAGATGCCGCACACAAACAATGCAAACGGGGGCAGG  
GGCGGGGGGGGGGGGGGGCAGAGGGCAGGGGGACGGGTGCGGACACCAGTGAAACTTGAAAC  
GGGAAGTGGGAGGACGTAGAGCAGAGAAGAGAACATTTTTTAAAAGGAAGGGATTAAAGAG  
GGTGGGAAATCTATGGTTTTTTATTTTAAAAAAG

SEQ ID NO: 69\_DYRK3\_H

CGGGAGCGAAAGTGCGCTGAGCTGCAGTGTCTGGTTCGAGAGTACCCGTGGGAGCGTCGCG  
CCGCGGAGGCAGCCGTCCCGGCGTAGGTGGCGTGGCCGACCGGACCCCCAACTGGCGCCT  
CTCCCCGAGCGGGGTCCCGAGCTAGGAGATGGGAGGCACAGCTCGTGGGCCTGGGCGGAA  
GGATGCGGGGGCCGCTGGGGCCGGGCTCCCGCCCCAGCAGCGGAGTTGGGGGATGGTGTC  
TATGACACCTTCATGATGATAGATGAAACCAAATGTCCCCCTGTTCAAATGTACTCTGC  
AATCCTTCTGAACCACCTCCACCCAGAAGACTAAATATGACCGCTGAGCAGTTTACAGGA  
GATCATACTCAGCACTTTTTTGGATGGAGGTGAGATGAAGGTAGAACAGCTGTTTCAAGAA  
TTTGGCAACAGAAAATCCAATACTATTTCAGTCAGATGGCATCAGTGACTCTGAAAAATGC  
TCTCCTACTGTTTCTCAGGGTAAAAGTTCAGATTGCTTGAATACAGTAAAATCCAACAGT  
TCATCCAAGGCACCCAAAGTGGTGCCTCTGACTCCAGAACAAGCCCTGAAGCAATATAAA  
CACCACCTCACTGCCTATGAGAACTGGAAATAATTAATTATCCAGAAATTTACTTTGTA  
GGTCCAAATGCCAAGAAAAGACATGGAGTTATTGGTGGTCCCAATAATGGAGGGGTATGAT  
GATGCAGATGGGGCCTATATTTCATGTACCTCGAGACCATCTAGCTTATCGATATGAGGTG  
CTGAAAATTATTGGCAAGGGGAGTTTTTGGGCAGGTGGCCAGGGTCTATGATCACAACTT  
CGACAGTACGTGGCCCTAAAAATGGTGCGCAATGAGAAGCGCTTTCATCGTCAAGCAGCT  
GAGGAGATCCGGATTTTGGAGCATCTTAAGAAACAGGATAAACTGGTAGTATGAACGTT  
ATCCACATGCTGGAAAGTTTCACATTCCGGAACCATGTTTGCATGGCCTTTGAATTGCTG  
AGCATAGACCTTTATGAGCTGATTAAAAAAAATAAGTTTCAGGGTTTTAGCGTCCAGTTG  
GTACGCAAGTTTGCCCAGTCCATCTTGCAATCTTTGGATGCCCTCCACAAAAATAAGATT  
ATTCATGCGATCTGAAGCCAGAAAACATTCTCCTGAAACACCACGGGCGCAGTTCAACC  
AAGGTCATTGACTTTGGGTCCAGCTGTTTTCGAGTACCAGAAGCTCTACACATATATCCAG  
TCTCGGTTCTACAGAGCTCCAGAAATCATCTTAGGAAGCCGCTACAGCACACCAATTGAC  
ATATGGAGTTTTTCGCTGCATCCTTGCAAGACTTTTAACAGGACAGCCTCTCTTCCCTGGA  
GAGGATGAAGGAGACCAGTTGGCCTGCATGATGGAGCTTCTAGGGATGCCACCACCAAAA  
CTTCTGGAGCAATCCAAACGTGCCAAGTACTTTATTAATTCCAAGGGCATACCCCGCTAC  
TGCTCTGTGACTACCCAGGCAGATGGGAGGGTTGTGCTTGTGGGGGGTTCGCTCACGTAGG  
GGTAAAAAGCGGGGTCCCCCAGGCAGCAAAGACTGGGGGACAGCACTGAAAGGGTGTGAT  
GACTACTTGTTTATAGAGTTCTTGAAAAGGTGTCTTCACTGGGACCCCTCTGCCCGCTTG  
ACCCAGCTCAAGCATTAAGACACCCTTGGAATTAGCAAGTCTGTCCCCAGACCTCTCACC  
ACCATAGACAAGGTGTCAGGGAAACGGGTAGTTAATCCTGCAAGTGCTTTCCAGGGATTG  
GGTTCTAAGCTGCCTCCAGTTGTTGGAATAGCCAATAAGCTTAAAGCTAACTTAATGTCA  
GAAACCAATGGTAGTATACCCCTATGCAGTGTATTGCCAAAACCTGATTAGCTAGTGGACA  
GAGATATGCCCAGAGATGCATATGTGTATATTTTTATGATCTTACAAACCTGCAAATGGA  
AAAAATGCAAGCCCATTCGTGGATGTTTTTGTAGAGTAGACTTTTTTTTAAACAAGACAA  
AACATTTTTTATATGATTATAAAGAATTCTTCAAGGGCTAATTACCTAACCAAGCTTGTA  
TGGCCATCTGGAATATGCATTAAATGACTTTTTTATAGGTCA



## FIGURE 2FFF

SEQ ID NO: 70\_AA589241\_M\_DYRK3\_M

CCACCGCTCCGGAGTTGCTAGGAATGCCACCGCAGAACTTCTGGAGCAATCCAAGCGTG  
CCAAGTACTTTATTAACTCCAAAGGCTTGCTTCGATACTGCTCCGTATCTACCCAGACGG  
ACGGGAGGGTGGTGCTTCTCGGGGGTCTGCTCACGCAGGGGTAAAAAGCGAGGCCCGCCAG  
GCAGCAAAGACTGGGCAACCGCACTGAAGGGCTGTGGTGACTACTTGTTTCATAGAGTTTC  
TGAAACGATGCCTCCAGTGGGACCCCTCTGCCCCGCTCACCCCGGCTCAAGCATTAAGAC  
ATCCTTGGATTAGCAAGTCTACACCCAAACCTCTCACCATGGACAAGGTGCCAGGGAAGC  
GGGTAGTTAACCCTACAAATGCTTTCCAGGGACTGGGTTCCTAAGCTGCCTCCAGTCGTTG  
GGATAGCCAGTAAGCTTAAAGCTAACCTAATGTCCGAAACCAGTGGTAGTATACCTCTGT  
GCAGTGTATTGCCAAAGCTGATTAGCTAGTGGACCACTCAGAGACTGATACATATCATAT  
GTATTTTAAATTACCTTGCAAACATGCAAATGGAAAACGGAATAATTGAAGCCCATTAC  
TGATGGATATGTTTTTGTAGACTTTTTTTTAAACAAGGCAGAACATTTTTTATATGACTAT  
AAAAGAACGCTTCAAGGGCTAATGTCAAACCAGCTTGTATTGGCCATCTGGAGTATACAT  
TAAATGACTTTTTTCATAGGTC

SEQ ID NO: 71\_5R72\_16\_2\_H

GTCGAGGCGCAGCGCTGCCATGGCTGGGGGCGCTGGGGCCCCCGGGCGCGGCCGGGACGA  
GCCTCCGGAGAGCTACCCGCAACGACAGGACCACGAGCTACAGGCCCTGGAGGCCATCTA  
CGGCGCGGACTTCCAAGACCTGCGGGCCGACGCTTGCGGACCGGTCAAAGAGCCCCCTGA  
AATCAATTTAGTTTTGTACCCTCAAGGCCTAACTGGTGAAGAAGTATATGTAAAAGTGGA  
TTTGAGGGTTAAATGCCACCTACCTATCCAGATGTAGTTCTGAAATAGAGTTAAAAAA  
TGCCAAAGGTCTATCAAATGAAAGTGTCAATTTGTAAAATCTCGCCTAGAAGAACTGGC  
CAAGAAACACTGTGGGGAGGTGATGATCTTTGAACTGGCTTACCACGTGCAGTCATTTCT  
CAGCGAGCATAACAAGCCCCCTCCCAAGTCTTTTCATGAAGAAATGCTGGAAAGGCGGGC  
TCAGGAGGAGCAGCAGAGGCTGTTGGAGGCCAAGCGGAAAGAAGAGCAGGAGCAACGTGA  
AATCCTGCATGAGATTCAGAGAAGGAAAGAAGAGATAAAAGAAGAGAAAAAAAGGAAAGA  
AATGGCTAAGCAGGAACGTTTGGAATTTGCTAGTTTGTCAAACCAAGATCATACCTCTAA  
GAAGGACCCAGGAGGACACAGAACGGCTGCCATTCTACATGGAGGCTCTCCTGACTTTGT  
AGGAAATGGTAAACATCGGGCAAACCTCCTCAGGAAGGTCTAGGCGAGAACGTCAGTATTC  
TGTATGTAATAGTGAAGATTCTCCTGGCTCTTGTGAAATTCTGTATTTCAATATGGGGAG  
TCCTGATCAGCTCATGGTGCACAAAGGGAAATGTATTGGCAGTGATGAACAACCTTGGAAA  
ATTAGTCTACAATGCTTTGGAAACAGCCACTGGTGGCTTTGTCTTGTGTATGAGTGGGT  
CCTTCAGTGGCAGAAAAAAATGGGTCCATTCTTACCAGTCAAGAAAAAGAGAAGATTGA  
TAAGTGCAAAAAGCAGATTCAAGGAACAGAAACAGAATTCAACTCACTGGTAAAATTGAG  
CCATCCAAATGTAGTACGCTACCTTGCAATGAATCTCAAAGAGCAAGACGACTCCATCGT  
GGTGGACATTTTAGTGGAGCACATTAGTGGGGTCTCTCTTGCTGCACACCTGAGCCACTC  
AGGCCCCATCCCTGTGCATCAGCTTCGCAGGTACACAGCTCAGCTCCTGTCAGGCCTTGA  
TTATCTGCACAGCAATTCTGTGGTGCATAAGGTCTTGAGTGCATCTAATGTCTTGGTGGGA  
TGCAGAAGGCACCGTCAAGATTACGGACTATAGCATTTCTAAGCGCCTCGCAGACATTTG  
CAAGGAGGATGTGTTTGAGCAAACCCGAGTTCGTTTTAGTGACAATGCTCTGCCTTATAA  
AACGGGGAAGAAAGGAGATGTTTGGCGTCTTGGCCTTCTGCTGCTGTCCCTCAGCCAAGG  
ACAGGAATGTGGAGAGTACCCTGTGACCATCCCTAGTGACTTACCAGCTGACTTTCAAGA  
TTTTCTAAAGAAATGTGTGTGCTTGGATGACAAGGAAAGATGGAGTCCCCAGCAGTTGTT  
GAAACACAGCTTTATAAATCCCCAGCCAAAAATGCCTCTAGTGGAACAAAGTCCTGAAGA  
TTCTGGAGGACAAGATTATGTTGAGACTGTTATTCTTAGCAACCGGCTACCCAGTGCTGC  
CTTCTTTAGTGAGACACAGAGACAGTTTTTCCCGATACTTCATTGAGTTTGAAGAATTACA  
ACTTCTTGGTAAAGGAGCTTTTGGAGCTGTCATCAAGGTGCAGAACAAGTTGGACGGCTG  
CTGCTACGCAGTGAAGCGCATCCCCATCAACCCGGCCAGCCGGCAGTTCCGCAGGATCAA  
GGGCGAAGTGACACTGCTGTACGGCTGCACCATGAGAACATTGTGCGCTACTACAACGC  
CTGGATCGAGCGGCACGAGCGGCCGGGGGACCGGGGACGGCGCCCCCGGACTCCGGGGC



## FIGURE 2GGG

CCTGGCCAAGGATGACCGAGCTGCACGCGGGCAGCCGGCGAGCGACACAGACGGCCTGGA  
CAGCGTAGAGGCCCGCCGCGCCGCCACCCATCCTCAGCAGCTCGGTGGAGTGGAGCACTTC  
GGGCGAGCGCTCGGCCAGTGCCCGTTTCCCCGCCACCGGGCCCGGGCTCCAGCGATGACGA  
GGACGACGACGAGGACGAGCAGCGGTGGCGTCTTCTCCAGTCCTTCCCTGCCTGCTTCAGA  
TTCTGAAAGTGATATTATCTTTGACAATGAAGATGAGAACAGTAAAAGTCAGAATCAGGA  
TGAAGATTGCAATGAAAAGAATGGCTGCCATGAAAGTGAGCCATCAGTGACGACTGAGGC  
TGTGCACTACCTATACATCCAGATGGAGTACTGTGAGAAGAGCACTTTACGAGACACCAT  
TGACCAGGGACTGTATCGAGACACCGTCAGACTCTGGAGGCTTTTTTCGAGAGATTCTGGA  
TGGATTAGCTTATATCCATGAGAAAGGAATGATTCACCGGGATTTGAAGCCTGTCAACAT  
TTTTTTGGATTCTGATGACCATGTGAAAATAGGTGATTTTGGTTTGGCGACAGACCATCT  
AGCCTTTTCTGCTGACAGCAAACAAGACGATCAGACAGGAGACTTGATTAAGTCAGACCC  
TTCAGGTCACCTTAAGTGGGATGGTTGGCACTGCTCTCTATGTAAGCCCAGAGGTCCAAGG  
AAGCACCAAATCTGCATACAACCAGAAAGTGGATCTCTTCAGCCTGGGAATTATCTTCTT  
TGAGATGTCCTATCACCCCATGGTTCACGGCTTCAGAAAGGATCTTTGTTCTCAACCAACT  
CAGAGATCCCACCTTCGCCTAAGTTTCCAGAAGACTTTGACGATGGAGAGCATGCAAAGCA  
GAAATCAGTCATCTCCTGGCTGTTGAACCACGATCCAGCAAACGGCCCACAGCCACAGA  
GCTGCTCAAGAGTGAGCTGCTGCCCCCACCACAGATGGAGGAGTCAGAGCTGCATGAAGT  
GCTGCACCACACGCTGACCAACGTGGATGGGAAGGCCTACCGCACCATGATGGCCCAGAT  
CTTCTCGCAGCGCATCTCCCCTGCCATCGATTACACCTATGACAGCGACATACTGAAGGG  
CAACTTCTCAATCCGTACAGCCAAGATGCAGCAGCATGTGTGTGAAACCATCATCCGCAT  
CTTTAAAAGACATGGAGCTGTTCAAGTTGTGTACTCCACTACTGCTTCCCCGAAACAGACA  
AATATATGAGCACAACGAAGCTGCCCTATTTCATGGACCACAGCGGGATGCTGGTGATGCT  
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GATCCCAGAAGATAAACTCAGTCAAGTCTACATTATTCTGTATGATGCTGTGACAGAGAA  
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GTGTCGACTCTACAAGTTTATTGAACAGAAGGGAGATTTGCAAGATCTTATGCCAACAAT  
AAATTCATTAATAAAACAGAAAACAGGTATTGCACAGTTGGTGAAGTATGGCTTAAAAGA  
CCTAGAGGAGGTTGTTGGACTGTTGAAGAACTCGGCATCAAGTTACAGGTCTTGATCAA  
TTTGGGCTTGGTTTACAAGGTGCAGCAGCACAATGGAATCATCTTCCAGTTTGTGGCTTT  
CATCAAACGAAGGCAAAGGGCTGTACCTGAAATCCTCGCAGCTGGAGGCAGATATGACCT  
GCTGATTCCCCAGTTTAGAGGGCCACAAGCTCTGGGGCCAGTTCCCACTGCCATTGGGGT  
CAGCATAGCTATAGACAAGATATCTGCTGCTGTCTCAACATGGAGGAATCTGTTACAAT  
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CCTAACCCAGAAACTCTGGACAGCAGGCATCACAGCAGAAATCATGTACGACTGGTCACA  
GTCCCAAGAGGAATTACAAGAGTACTGCAGACATCATGAAATCACCTATGTGGCCCTTGT  
CTCGGATAAAGAAGGAAGCCATGTCAAGGTTAAGTCTTTCGAGAAGGAAAGGCAGACAGA  
GAAGCGTGTGCTGGAGACTGAACTTGTGGACCATGTACTGCAGAACTGAGGACTAAAGT  
CACTGATGAAAGGAATGGCAGAGAAGCTTCCGATAATCTTGCAGTGCAAAATCTGAAGGG  
GTCATTTTCTAATGCTTCAGGTTTGTGTTGAAATCCATGGAGCAACAGTGGTTCCCATTTGT  
GAGTGTGCTAGCCCCGGAGAAGCTGTGAGCCAGCACTAGGAGGCGCTATGAAACTCAGGT  
ACAAACTCGACTTCAGACCTCCCTTGCCAACTTACATCAGAAAAGCAGTGAAATTGAAAT  
TCTGGCTGTGGATCTACCCAAAGAAACAATATTACAGTTTTTTATCATTAGAGTGGGATGC  
TGATGAACAGGCATTTAACACAACCTGTGAAGCAGCTGCTGTACGCCTGCCAAAGCAAAG  
ATACCTCAAATTAGTCTGTGATGAAATTTATAACATCAAAGTAGAAAAAAAGGTGTCTGT  
GCTATTTCTGTACAGCTATAGAGATGACTACTACAGAATCTTATTTTAACCCTAAAGAAC  
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TCATCATAATTTAAAATTAAATTCTAAGAAGAGGCTGGGTGCAGTGGCTCACACCTTTAA  
TCCCAGCACTTTGGGAAGCCAAGGCAGGAAGACTGCTTGAAACCAGGAGTTTGAGACCAG  
CCT

ATGCTGGGGGGGCA<sup>-</sup>ACTCCGGGGTCCGCA<sup>-</sup>AAGCGCGAAGAGGGAGGGCGACGGGGGCTGGGGGCT  
GTGGCTGCGCCCGCCGGCCATCGACTTTCCCGCCGAGGGCCCGGACCCCGAATATGACGAA  
TCTGATGTTCCAGCAGAAATCCAGGTGTTAAAAGAACCCCTACAACAGCCAACCTTCCCT  
TTTGCAGTTGCAAACCAACTCTTGCTGGT<sup>-</sup>TTCTTTGCTGGAGCACTTGAGCCACGTGCAT  
GAACCAAACCCACTTCGTTCAAGACAGGTGTTTAAGCTACTTTGCCAGACGTTTATCAAA  
ATGGGGGCTGTTGTCTTCTTTCACTTGTAGTGACGAGTTTAGCTCATTGAGACTACATCAC  
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CTTCAGCACCCCAATATTGTTGGCTATCACACCGCGTGGATAGAACATGTTTCATGTGATT  
CAGCCACGAGCAGACAGAGCTGCCATTGAGTTGCCATCTCTGGAAGTGCTCTCCGACCAG  
GAAGAGGACAGAGAGCAATGTGGTGT<sup>-</sup>TAAAAATGATGAAAGTAGCAGCTCATCCATTATC  
TTTGCTGAGCCCACCCCAAGAAAAAGAAAAACGCTTTGGAGAATCTGACACTGAAAATCAG  
AATAACAAGTCGGTGAAGTACACCACCAATTTAGTCATAAGAGAATCTGGTGA<sup>-</sup>ACTTGAG  
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CAGCAGCTGCCACTCAGGCGTAATTCCCACCTAGAGGAGAGTTTCACATCCACCGAAGAA  
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CGGGGCGGGGAGTATGTGGACGAGTCTGCCTGTCCTTATGTTATGGCCAATGTTGCAACA  
AAAATTTTTTCAAGAATTGGTAGAAGGTGTGTTTTTACATACATAACATGGGAATTGTGCA<sup>-</sup>C  
CGAGATCTGAAGCCAAGAAATATTTTTCTTCATGGCCCTGATCAGCAAGTAAAAATAGGA  
GACTTTGGTCTGGCCCTGCACAGACATCCTACAGAAGAACACAGACTGGACCAACAGAAAC  
GGGAAGAGAAACACCAACACATACGTCCAGAGTGGGTACTTGTCTGTACGCTTCACCCGAA  
CAGTTGGAAGGATCTGAGTATGATGCCAAGTCAGATATGTACAGCTTGGGTGTGGTCCTG  
CTAGAGCTCTTTCAGCCGTTTGGAAACAGAAATGGAGCGAGCAGAAGTTCTAACAGGTTTA  
AGAACTGGTCAGTTGCCGGAATCCCTCCGTAAAAGGTGTCCAGTGCAAGCCAAGTATATC  
CAGCACTTAACGAGAAGGAACTCATCGCAGAGACCATCTGCCATTGAGCTGCTGCAGAGT  
GAACTTTTCCAAAATTCTGGAAATGTTAACCTCACCTACAGATGAAGATAATAGAGCAA  
GAAAAAGAAATTGCAGAACTAAAGAAGCAGCTAAACCTCCTTTCTCAAGACAAAGGGGTG  
AGGGATGACGGAAAGGATGGGGGCGTGGGATGA

CACAAGAGCCCTTCTCTGCAGGGAACCTCAGGCTTCAGAGAGCCGAAAAGTTGGGAGGCGT  
AACCACCTTACAGGCCGGAAGTGTCCGGGGTGGACGCATTCGGGTAGCCGAAGAAGTCCCA  
GGATTGCCGAAGAAGTCCCAGGATTTCCGAAGCGAGCCGAAGCATCGCGACAGTTTTTCAG  
AGACAGCTGATCGGTTGGAGCTGTTGCGCCGAGCAGTCATGGCGGCGGCCAGAGCTACTA  
CGCCGGCCGATGGCGAGGAGCCCCGCCCCGGAGGCTGAGGCTCTGGCCGCAGCCCCGGGAGC  
GGAGCAGCCGCTTCTTGAGCGGCCCTGGAGCTGGTGAAGCAGGGTGCCGAGGCGCGCGTGT  
TCCGTGGCCGCTTCCAGGGCCGCGCGGCGGTGATCAAGCACCGCTTCCCCAAGGGCTACC  
GGCACCCGGCGCTGGAGGCGCGGCTTGGCAGACGGCGGACGGTGCAAGGAGGCCCGGGCGC  
TCCTCCGCTGTCGCCGCGCTGGAATATCTGCCCCAGTTGTCTTTTTTTGTGGACTATGCTT  
CCAACTGCTTATATATGGAAGAAATTGAAGGCTCAGTGACTGTTGAGATTATATTCACT  
CCACTATGGAGACTGAAAAAACTCCCCAGGGTCTCTCCAACTTAGCCAAAGACAATTGGGC

## FIGURE 2III

AGGTTTTGGCTCGAATGCACGATGAAGACCTCATTCATGGTGATCTCACCACCTCCAACA  
TGCTCCTGAAACCCCCCTGGAACAGCTGAACATTGTGCTCATAGACTTTGGGCTGAGTT  
TCATTTTCAGCACTTCCAGAGGATAAGGGAGTAGACCTCTATGTCCTGGAGAAGGCCTTCC  
TCAGTACCCATCCCAACACTGAAACTGTGTTTGAAGCCTTTCTGAAGAGCTACTCCACCT  
CCTCCAAAAAGGCCAGGCCAGTGCTAAAAAAATTAGATGAAGTGCGCCTGAGAGGAAGAA  
AGAGGTCCATGGTTGGGTAGAAGAATGTGTATGACAACCACACACAGTGAAGCTCTTTTT  
TCAAAGTAAATTTGAAGAAATGCTACAAGTATGAGATGAGATCTAAGTAAAGGTGTTAAG  
ATATTTTTTAAGTGGTATGTGATCGTGTCATTATCATCTGCACTTCACTCAAGAGCTTACT  
ATGTGTCTAAGTCATGTTCTAGGCAGAATTGGGTATTTAAAGTAAATTGAGGACAGGCTT  
CTCCAGATTGTGACATGTATATCTCAGATACATGGGTGTGGCATTGAACCACATAATGA  
GAACATTATTCTCTTTTTAGTCCTTGTGAGACAAGGATGAAGTCTCAGTTGCTGATACTC  
GCTGAGCTTACTGGCCCTCTAACCCAGTGTTTTTTTTTTTGTGTTGTTGTGTACATGTTAT  
ATTTATTTTGAAACCAGTTTAATGGGATACAACCAGCATTTTAAAAAATGAAATAGAATA  
CAGCATGGAAAATATCAGTGTATTGTTTTTATGAACTTTTCAGTGTATATATAGACCAAG  
GATATGTGCTGAGTTTTGATGTCAAATATATTTCTCTTTCAGGGTCATGATCAAAAAATG  
AAAAGTCTGCTTAACCTCCAATTTCTCTTTTAAAAAAGCAGACTTACAGCTTTCAGGCAAC  
TGAAATTCATGTTAACATGTTTTTATTTTTTATTGCTTTGTATTTTTTGTGGTTACCTTCTA  
AGACAAGTGATTGATCTAAAGTTCCTTTTAAGTTTATACCGCTAAACAAACTGAGTTGAT  
TTCTATCACAGGCAGTAAGTAGGTAGAGCAAAAATGGTGAAGTGAAGTGTGAAGACTGAA  
GTTTGATGAAGTCTGGTTTAAGGCACAGGTAAACTGAGTGTGGATGCAAAAGTACCAGGA  
GCTAGCTTTTAACCTTGCCAGCCTCAGTTTCTTTTCTTAGAAGAAGCTATGTTTGGGTG  
GGAAGGGAAGAGAGGGATAAGAAAATACCTTTCTTCCTTGTAACCTCCAATCAACAAACA  
TATTTTGAGTGCCTTTTGTGTTCCCTTGGCACCCTGTTGGGTATTGGGTACTTGGCACCCT  
GTTGGGTATTGGGTACAATGGTGAGCCAGACAGACACAGCGCCTGTCCTTTTGTAAGAAT  
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TGATTGCTACAGCTGAGCTAATTAACACCCATCACCTCACATAGTTACTGTCTTGTTTCT  
TAATATGGACATTTGCAGCTATGAATTTCCCTCTGCACACTGTTGTCATCACACACTCTC  
AGTTTTTGGTATTTTTGTGTTTTTGTTCATTTCATCTCAAAGTATTTTCTAATTTCCCTTG  
TGATTTCTTCTTTGACCCCTTGATTGTTTAGAAATCTGTTAATTTCCACACATTTGTAAA  
TGTTCCAATTTTTCTTTTGTATTGCCAGCTTCATTCCATTGTGTTTCAGAGATGATACAG  
TCAGTGCCTGTTCTTATGAAGCAAACATTCTATAATAGTAGGACCAGTACCCTGTCTGTT  
TCATTCACCACAGTCAGCATGCCCAAGTGCCAGCATGGGGCGGATGGCCAGGAATGAG  
TGAAAACCTCCCTTCCTGGGTAGTTGTGACTAGTAGAGAGGAAAAAFAATATAATTGCCT  
GCTTACTGCATGCCAGGCATTGGGCTGGGAATTTTTTATATTGGATCTAAAATAACTCTTA  
AGTTAGGCATTATCCCCATTTTATAGATGGAGAACTGGCCCCAAAAGGTGGGAACTTGT  
CCAAGACGTCACAGGTAGCAAGAGGTACTTTTACCTGGCTCCAAATCTGTGTTCTTTCCA  
CTGACAAATGAGATATGGGATATGGTGCATCTTTACAGTACTATAATAAGTATTGGCGTA  
TAACATTATTTTCAAGGAACTCCAAGGGCCACAGGAGCTGACAGGTTTTTCAATTAATAT  
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CCTGCTTTGTTGGGGTATGGTTGGCTCGTGTGCATTAAGTCAACAAATCCCTAGT

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CTGGTGCAGCAGGGCGCCGAGGCGCGCGTTTTCCGTGGCCGCTTCCAGGGCCGCGCGGCC  
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CGTCGGCGGACGGTGCAGGAGGCGCGCGCGCTGCTCCGCTGCCGCCGTGCGGGGATAGCT  
GCCCCAGTCGTCTTCTTTGTGGACTATGCGTCTAACTGCTTATATATGGAAGAAATCGAA  
GACTCGGTGACTGTTCTGGGATTATATCCAATCCACTATGGAGACTGAAAAGGACCCCCAG  
TGCTTCTTGGACCTGGCCAGGAGGATGGGGCAGGTCTGGCCGGAATGCACGACCAAGAC  
CTCATTACGGGGACCTCACACCTCCAACATGCTCCTGAGGCGGCCCTGGCGCAGCTG  
CACATCGTGCTCATCGACTTTGGGCTGAGCTTTGTCTCAGGACTGCCGGAAGATAAAGGC



## FIGURE 2JJJ

GTCGACCTCTATGTCCTGGAGAAGGCCTTCCTCAGCACGCACCCCCACACCGAGACCGCG  
TTTGAAGCCTTTCTGAAGAGTTACGGGGCCTCGTCCAAGAAGTCCAGTCCAGTGCTGAAG  
AAGTTAGATGAGGTGCGCCTGAGAGGGCGAAAGCGGTCCATGGTTCGGGTAGTGAGAGCTGT  
GGTGAACCTGGCTCACGGTGAAGGATGATGTAGACGAGGCTGGACCCCTCAGCAAAGCATG  
GGTTGTAAAGTGGTCTGTGATCGTGCTGGGCCACCACCATCCATGGCTCACTGTTCTCAG  
GGGCTTCATGTACATGAGGTTTATTCTGGGCAGAACTGGGTAGGTAGCCCAGGCTAGCCT  
TGAATTTATGGCAACATCCTACCTCAGCTTGCTTGGAAGAGGTTATAAGCCACCATACTT  
GACTTTGCACTGATTCTGTCAGAAAC

SEQ ID NO: 76\_17000139801197\_H, IRAKM\_H

ATGGCGGGGAACTGTGGGGCCCCGCGGCGCGCTGTCGGCGCACACGCTGCTGTTGACCTG  
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TGGCGCGGCCTGGCAGAGAGACTTTCAAGCAGCTGGCTGGATGTTTCGTCATATTGAAAAG  
TATGTAGACCAAGGTAAAAGTGGAACAAGAGAATTACTTTGGTCCTGGGCACAGAAAAAC  
AAGACCATCGGTGACCTTTTACAGGTCCTCCAGGAGATGGGACATCGTCGAGCTATTCAT  
TTAATTACAAACTATGGAGCAGTGTTGAGTCCTTCAGAGAAGAGTTATCAGGAAGGTGGA  
TTTCCAAATATATTATTCAAGGAAACAGCCAATGTCACCGTGGATAATGTTCTTATTCT  
GAACATAATGAAAAAGGAGTACTGCTTAAATCTTCCATCAGCTTTCAAATATCATAGAA  
GGAAGTAGAAATTTCCACAAAGACTTCCTAATTGGAGAAGGAGAGATTTTTGAGGTATAC  
AGAGTGGAGATTCAAACCTAACATATGCTGTCAAATTATTTAAACAGGAGAAAAAATG  
CAGTGTAAGAAGCATTGGAAGAGGTTTTTATCTGAGCTTGAAGTTTTACTACTGTTTCAT  
CACCCAAACATACTAGAGTTGGCTGCATATTTTACAGAGACTGAGAAGTTCTGTCTGATT  
TATCCATACATGAGAAATGGAACACTTTTTGACAGATTGCAGTGTGTAGGTGACACGGCC  
CCACTCCCTTGGCACATTCGAATCGGTATATTAATAGGAATATCCAAAGCCATTCACTAC  
CTGCACAACGTTCAACCATGCTCGGTCACTGTGGCAGTATATCAAGTGCAAACATCCTT  
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CTAGAACATCAGAGTTGTACCATAAATATGACCAGCAGCAGCAGTAAACATCTGTGGTAC  
ATGCCAGAAGAGTACATCAGACAGGGGAACTTTCCATTAAAACAGATGTCTACAGCTTT  
GGAATTGTAATAATGGAAGTTCTAACAGGATGTAGAGTAGTGTTAGATGATCCAAAACAT  
ATCCAGCTGCGGGATCTCCTTAGAGAATTGATGGAGAAGAGAGGCCTGGATTGATGCTCTC  
TCATTTCTAGATAAGAAAGTGCCTCCCTGCCCTCGGAATTTCTCTGCCAAGCTCTTCTGT  
TTGGCAGGCCGGTGTGCTGCAACGCGGGCAAAGTTAAGACCATCAATGGATGAAGTTTAA  
AATACTCTTGAAAGTACTCAAGCCAGCTTGTATTTTGCTGAAGATCCTCCCACATCACTA  
AAGTCCTTCAGGTGTCCTTCTCCTCTATTCTGAGAAATGTACCAAGTATTCCAGTGGA  
GATGATGAAAGCCAGAATAACAATTTACTACCTTCTGATGAAGGCCTGAGGATAGACAGA  
ATGACTCAGAAAACCTCTTTTGAATGCAGCCAGTCTGAGGTTATGTTTCTGAGCTTGGAC  
AAAAAGCCAGAGAGCAAGAGAAATGAGGAAGCTTGCAACATGCCAGTTCTTCTTGTGAA  
GAAAGTTGGTTCCCAAAGTATATAGTTCCATCCCAGGACTTAAGGCCCTATAAGGTAAAT  
ATAGATCCTTCTTCAGAAGCTCCAGGGCATTCTTGCAGGAGCAGGCCAGTGGAGAGCAGC  
TGTTCTCCAAATTTTCTGCGGATGAATATGAACAGTACAAAAAAGAATAA

SEQ ID NO: 77\_AA840598\_M IRAKM\_M

ATGTGGAAGAGATTTTTATCAGAACTGGAAGTTCTACTCCTGTTCCGTCACCCCCACATA  
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AGCAACGGGACGCTTTTCGACAGATTACAGTGCACAAATGGCACAACCCCGCTTTCCTGG  
CACGTTTGAATCAGCGTATTGATAGGAATAGCCAAAGCCATCCAATACTTGACACAACACT  
CAGCCGTGCGCCGTCATCTGTGGCAACGTTTCCAGTGCAAAACATACTCTTGGATGACCAG  
CTCCAACCCAACTAACGGATTTTGCTGCAGCGCACTTCCGACCCCAATCTAGAGCAGCAG  
AGTTCTACCATAAATATGACCGGGCGGTGGCAGGAAACATCTGTGGTACATGCCAGAAGAA

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## FIGURE 2KKK

TACATCAGACAGGGAAGACTTTCCGTTAAAACTGATGTCTACAGCTTCGGAATCGTGATC  
ATGGAGGTTCTAACGGGCTGCAAAGTGGTGCTGGATGACCCGAAACACGTTTCAGCTGCGG  
GACCTCCTCATGGAAGTGTGGAGAAAAGAGGGCCTAGACTCCTGCCTGTCCTTCTTAGAC  
AGGAAGATACCACCCTGTCCTCGGAAGTCTCTGCAAAGCTCTTCTCTCTGGCGGGCCGG  
TGTGTGGCAACGAAGGCCAAGTTAAGACCCACGATGGACGAAGTCCTGTCCTCTCTGGAG  
AGCACCCAGCCTAGCTTGTATTTTGCAGAAGACCCTCCACGTCCTTGAAGTCCTTCAGG  
TGTCTTCTCCACTGTTCTTGGATAATGTCCCAAGTATTCCAGTAGAAGATGATGAAAAC  
CAGAATAACCATTCAGTACCTCCCAAGGAAGTTTGGGGACAGATAGAGTGACTCAGAAA  
ACCCCTTTGAATGCAGCCAGTCTGAGGTACCTTTCTAGGCTTGGACCGAAACAGAGGG  
AACAGGGGAAGTGAAGCGGATTGCAACGTGCCAGTTCTTCTCATGAGGAATGCTGGTCC  
CCAGAGCTTGTGGCGCCATCCCAGGACTTAAGTCCTACTGTGATCAGTTTGGGCTCGTCT  
TGGGAAGTACCAGGCCATTCTTATGGGAGCAAGCCAATGGAGAAGAGGTGTTCTCTGGG  
CTCTTTTGCAGTGAGCATGAACAGTCCAAAAGCAGTGAATCCACCAGAAGATCAAGCAA  
AAAATAAAAGCAAACGTCCTGAAGGCACTGAGCAAATAGCATCCCCGTGAAAAGACACG  
AGCTCTGAGCTCCGTGAGTACAGCCAAGGGACCAACTGATGGAGAATTTGAATGGTGCAG  
ATTAGCAGCAAGGAAGTCTATTCCTTCCTCCAAACAGAATAATTTCAAGAGATGCTTTAT  
TCAAGTGACCGCCTCTCAGTCAAACCTGAGAAGCTAAACTGGAGCCAATCAGAATTATCC  
AAGATTCCGGGTCTGACAACCAAAACCTAGCAAAGAGTAGCAGGACAAGTCTCTCTCTT  
AAGTCTCTCACTCTCTCTCATCATCCGAGTGAGATCTTGGTATAGGTGAACAGAGAACCA  
CCCACCTTCCAGAACCAGAACCACCTTCTCCCCAAGCCAGCAGTCAGTCACTCACCATCA  
GCAGCCAGTAGTCACCAGCAGCCAATCATGATACAGTGTCACTCTCCCTCTGCGCATGCC  
CTACGTCCTTTATAAAACCCAGGTCTTCAGGGCCCCACCCCTTTCTTTTTCCATCCTTGCT  
CAGAGGCAGCCTTTTGTATACATTCCCTGACCCCAACCCCAATTATATCTCTCATATGATA  
TCTGTTGCGTAGTGTGACTTTGTGGCATGACTTGGTTGTCAGATCATTTGCACAAGAACA  
AGCGAATACACAACAACAAGCCCACCATCATTACCACCGGCACTTAATGCTAGTCTTTC  
TGCTAGGGATACTGACAGTCTATTTGCTTCCCATGGTCATAGGGAAGTTGCTCAAATGCA  
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TTTTACAGCCAGTTGCTACTCTTGTATTATCGCTGGTTAACCGGTCTGTCCGGAAGTGAGC  
CAAGTCATCCTTGCTAGGGCTTTTTCTGTGTAGAGAGGGAATTCCAGTCCAAAGTCTGCT  
TCTCTGTATTTAAATTCTTAGAAGAGTTGCCTGTGGCATTCCAATTGTTATATAAAAAA  
TTATATTAAAGAATTCCAGCACT

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ATGGCGAGTGCGGTGAGGGGGTGGAGGCCGTGGCCCCGGCTGGGGCTCCAGCTCCAGTTC  
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CTGCTGGTGTCCACCTTGGATGGAAGTCTCCACGCACTAAGCAAGCAGACAGGGGACCTG  
AAGTGGACTCTGAGGGATGATCCCGTCATCGAAGGACCAATGTACGTACAGAAATGGCC  
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GGGGAGACCCAGATGACACTGACCACAGAGGGTCCCTCCACCCCCCGCCTCTACATTGGC  
CGAACACAGTATACGGTCACCATGCATGACCCAAGAGCCCCAGCCCTGCGCTGGAACACC  
ACCTACCGCCGCTACTCAGCGCCCCCATGGATGGCTCACCTGGGAAATACATGAGCCAC  
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TGGACACAGGACCTGGGCGTGCCTGTGATGGGCGTCTACACCTGGCACCAGGACGGCCTG  
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GGCCACATCCGACTGCCTGCCTCAGGCCCCCCGGGACACAGCCACCCTCTTCTCTACCTTG  
GACACCCAGCTGCTAATGACGCTGTATGTGGGGAAGGATGAACTGGCTTCTATGTCTCT  
AAAGCACTGGTCCACACAGGAGTGGCCCTGGTGCCTCGTGGACTGACCCTGGCCCCCGCA  
GATGGCCCCACACAGATGAGGTGACACTCCAAGTCTCAGGAGAGCGAGAGGGCTCACCC

## FIGURE 2LLL

AGCACTGCTGTTAGATAACCCCTCAGGCAGTGTGGCCCTCCCAAGCCAGTGGCTGCTCATT  
GGACACCACGAGCTACCCCCAGTCCTGCACACCACCATGCTGAGGGTCCATCCCACCCCTG  
GGGAGTGGAAGTGCAGAGACAAGACCTCCAGAGAATAACCCAGGCCCCAGCCTTCTTCTTG  
GAGCTATTGAGCCTGAGCCGAGAGAACTTTGGGACTCCGAGCTGCATCCAGAAGAAAAA  
ACTCCAGACTCTTACTTGGGGCTGGGACCCCAAGACCTGCTGGCAGCTAGCCTCACTGCT  
GTCTCCTGGGAGGGTGGATTCTCTTTGTGATGAGGCAGGTGGTGGAGAAGCAGCAGGAG  
ACCCCCCTGGCACCTGCAGACTTTGCTCACATCTCCCAGGATGCCCAGTCCCTGCACTCG  
GGGGCCAGCCGGAGGAGCCAGAAGAGGCTTCAGAGTCCCTCAAAGCAAGCCCAGCCACTC  
GACGACCCTGAAGCTGAGCAACTCACCGTAGTGGGGAAGATTTCTTCAATCCCAAGGAC  
GTGCTGGGCCGCGGGGCAGGCGGGACTTTCGTTTTCCGGGGACAGTTTGAGGGACGGGCA  
GTGGCTGTCAAGCGGCTCCTCCGCGAGTGCTTTGGCCTGGTTCGGCGGGGAAGTTCAACTG  
CTGCAGGAGTCTGACAGGCACCCCAACGTGCTCCGCTACTTCTGCACCGAGCGGGGACCC  
CAGTTCCACTACATTGCCCTGGAGCTCTGCCGGGCCCTCCTTGCAAGGAGTACGTAGAAAAC  
CCGGACCTGGATCGCGGGGGTCTGGAGCCCGAGGTGCTGCTGCAGCAGCTGATGTCTGGC  
CTGGCCCACCTGCACTCTTTACACATAGTGACCCGGGACCTGAAGCCAGGAAATATTCTC  
ATCACCGGGCCTGACAGCCAGGGCCTGGGCAGAGTGGTGTCTCAGACTTCGGCCTCTGC  
AAGAAGCTGCCTGCTGGCCGCTGTAGCTTCAGCCTCCACTCCGGCATCCCCGGCACGGAA  
GGCTGGATGGCGCCCCGAGCTTCTGCAGCTCCTGCCACCAGACAGTCCCTACCAGCGCTGTG  
GACATCTTCTCTGCAGGCTGCGTGTCTACTACGTGCTTTCTGGTGGCAGCCACCCCTTT  
GGAGACAGTCTTTATCGCCAGGCAAACATCCTCACAGGGGCTCCCTGTCTGGCTCACCTG  
GAGGAAGAGGTCCACGACAAGGTGGTTGCCCGGGACCTGGTTGGAGCCATGTTGAGCCCA  
CTGCCGCAGCCACGCCCCCTCTGCCCCCAGGTGCTGGCCCACCCCTTCTTTTGGAGCAGA  
GCCAAGCAACTCCAGTTCTTCCAGGACGTGAGTACTGGCTGGAGAAGGAGTCCGAGCAG  
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GAGCACATCTCCATGCCGCTGCAGACAGATCTGAGAAAGTTCCGGTCCTATAAGGGGACA  
TCAGTGCGAGACCTGCTCCGTGCTGTGAGGAACAAGAAGCACCACTACAGGGAGCTCCCA  
GTTGAGGTGCGACAGGCACTCGGCCAAGTCCCTGATGGCTTCGTCCAGTACTTCACAAAC  
CGCTTCCCACGGCTGCTCCTCCACACGCACCGAGCCATGAGGAGCTGCGCCTCTGAGAGC  
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GGGAGGTGA

SEQ ID NO: 79\_HGP\_6644466

GGAGGGTTCGAATTGCAACGGCAGCTGCCGGGCGTATGTGTTGGTGCTAGAGGCAGCTGC  
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TTCACCTCCGACCTTTCCTTCCAGGCGGTGAGACTCTGGACTGAGAGTGGCTTTCACAAT  
GGAAGGGATCAGTAATTTCAAGACACCAAGCAAATTATCAGAAAAAAGAAATCTGTATT  
ATGTTCAACTCCAATATAAATATCCCGGCCTCTCCGTTTATGCAGAAGCTTGGCTTTGG  
TACTGGGGTAAATGTGTACCTAATGAAAAGATCTCCAAGAGGTTTGTCTCATTCTCCTTG  
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TGCTTTTACTGAAGCCAATGATGGCAGTCTGTGTCTTGCTATGGAATATGGAGGTGAAAA  
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CATAATTTTAAAGTTGCTTTGAATATGGCAAGAGGGTTAAAGTATCTGCACCAAGAAAA  
GAACTGCTTCATGGAGACATAAAGTCTTCAAATGTTGTAATTAAAGGCGATTTTGA AAC  
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CCCTGAGGCTTGTTACATTGGCACAGAGCCATGGAAACCCAAAGAAGCTGTGGAGGAGAA  
TGGTGTTATTACTGACAAGGCAGACA'TATTTGCCTTTGGCCTTACTTTGTGGGAAATGAT  
GACTTTTATCGATTCCACACATTAATCTTTCAAATGATGATGATGATGAAGATAAACTTT  
TGATGAAAGTGATTTTGTATGATGAAGCATACTATGCAGCGTTGGGAACTAGGCCACCTAT  
TAATATGGAAGAACTGGATGAATCATACCAGAAAGTAATTGAACTCTTCTCTGTATGCAC

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## FIGURE 2MMM

TAATGAAGACCCTAAAGATCGTCCTTCTGCTGCACACATTGTTGAAGCTCTGGAAACAGA  
TGTCTAGTGATCATCTCAGCTGAAGTGTGGCTTGCGTAAATAACTGTTTATTCCAAAATA  
TTTACATAGTTACTATCAGTÀGTTATTAGACTCTAAAATTGGCATATTTGAGGACCATAG  
TTTCTTGTTAACATATGGATAACTATTTCTAATATGAAATATGCTTATATTGGCTATAAG  
CACTTGGAATTGTAAGTGGGTTTTCTGTAAAGTTTTAGAACTAGCTACATAAGTACTTTG  
ATACTGCTCATGCTGACTTAAAACACTAGCAGTAAAACGCTGTAAACTGTAACATTAAAT  
TGAATGACCATTACTTTTATTAATGATCTTTCTTAAATATTCTATATTTTAAATGGATCTA  
CTGACATTAGCACTTTGTACAGTACAAAATAAAGTCTACATTTGTTTAAAACACTGAACC  
TTTTGCTGATGTGTTTATCAAATGATAACTGGAAGCTGAGGAGAATATGCCTCAAAAAGA  
GTAGCTCCTTGGATACTTCAGACTCTGGTTACAGATTGTCTTGATCTCTTGGATCTCCTC  
AGATCTTTGGTTTTTGGCTTTAATTTATTAAATGTATTTTCCATACTGAGTTTAAAATTTA  
TTAATTTGTACCTTAAGCATTTCCCAGCTGTGTAAAAACAATAAACTCAAATAGGATGA  
TAAAGAATAAAGGACACTTTGGGTACCAGAAGGTGTCTCAGCATTATTTTATACTTC

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ATCTCCAAGAGGGTTGTCTCATTCTCCTTGGGCGGTGAAAAAGATAAGTCTTTTATGCGA  
TGATCATTATCGAACTGTGTATCAGAAGAGACTAACTGATGAAGCTAAGATTTTAAAAAA  
CCTTAATCACCCAAACATTATAGGATATCGTGCTTTTACTGAAGCCAGTGATGGTAGTCT  
GTGCCTTGCTATGGAGTATGGAGGTGAAAAGTCTCTGAATGACTTAATAGAAGAGCGGAA  
CAAAGACAGTGGAAGTCCTTTTCCAGCAGCTGTAATTCTCAGAGTTGCTTTGCACATGGC  
CAGAGGGCTAAAGTACCTGCACCAAGAAAAGAAGCTGCTTCATGGAGACATAAAGTCTTC  
AAATGTTGTAATTAAAGGTGATTTTGAACAATTAAATCTGTGATGTAGGAGTCTCTCT  
GCCATTGGATGAAAATATGACTGTGACTGATCCTGAGGCCTGTTATATTGGTACTGAGCC  
ATGGAAACCCAAGGAAGCGTTGGAAGAAAATGGCATCATTACTGACAAGGCAGATGTGTT  
TGCTTTTGGCCTTACTCTGTGGGAAATGATGACTTTATGTATTCCACACGTCAATCTTCC  
AGATGATGATGTTGATGAAGATGCAACCTTTGATGAGAGTGACTTCGATGATGAAGCATA  
TTATGCAGCTCTGGGGACAAGGCCATCCATCAACATGGAAGAGCTGGATGACTCCTACCA  
GAAGGCCATTGAACTCTTCTGTGTGTGCACTAATGAGGATCCTAAAGATCGCCCGTCTGC  
TGCACACATCGTTGAAGCTTTTGAAGCTAGATGGCCAATGTTGTGGTCTAAGCTCAAAGCA  
TTAACTTGTATGGGAAGTGTAACTAGATATATGTAGTTAATATAACTTATGGTAGCTAG  
ATTCTAGAAGTAGCTTTAACACTAGTGACCCCTGTCTAAGATGACTTAAGAATCAAGGGA  
CCATTGCTTTGTTACAGATCTTTTTTAGATATTCTTGCTTCTTTAGTGGGTACTAAAAAT  
TTCACACGTACATGTGGTACAGATATCTGTCTGCTCATAGTGTGAGTCCTTCAGCTGGC  
CTGTCAGCCCATGCGCCCTGGGACTTGAGAAGAGTTCATAAACGTAGCTCCTAGGGTGTC  
TTGCCTCTCTACACTTAGCTTCTAATTTATTACTTTGTTTTCTACTGATTGTGTCTTAAGT  
CTTTTAAAATAAATGTAAGAATAAACAATAAAAGACAGTTTTTAGTACCAGG

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GCTGCTGGACAGTGACTTGTATTTACCGTGGACTGTGAGAGTGAACTGGCCTATGGCAT  
AGCAGTGGGCCTCAGCTACCTTCACTTCAAAGGCATTTTCCATCGGGACCTCACATCAAA  
GGTGTGAAGGCTTTGCTTTC

SEQ ID NO: 82\_AA232253\_H

ATGTCGTCTCTCGGTGCCTCCTTTGTGCAAATTAATTTGATGACTTGCAGTTTTTTTGAA  
AACTGCGGTGGAGGAAGTTTTTGGGAGTGTTTATCGAGCCAAATGGATATCACAGGACAAG  
GAGGTGGCTGTAAAGAAGCTCCTCAAAATAGAGAAAGAGGCAGAAATACTCAGTGTCTC  
AGTCACAGAAACATCATCCAGTTTTTATGGAGTAATTCTTGAACCTCCCAACTATGGCATT  
GTCACAGAATATGCTTCTCTGGGATCACTCTATGATTACATTAACAGTAACAGAAGTGAG  
GAGATGGATATGGATCACATTATGACCTGGGCCACTGATGTAGCCAAAGGAATGCATTAT  
TTACATATGGAGGCTCCTGTCAAGGTGATTACAGAGACCTCAAGTCAAGAAACGTTGTT



## FIGURE 2NNN

ATAGCTGCTGATGGAGTATTGAAGATCTGTGACTTTGGTGCCCTCTCGGTTCOCATAAOCAT  
ACAACACACATGTCCTTGGTTGGAACCTTTCCCATGGATGGCTCCAGAAGTTATCCAGAGT  
CTCCCTGTGTCAGAACTTGTGACACATATTCCTATGGTGTGGTTCTCTGGGAGATBCTA  
ACAAGGGAGGTCCCCCTTTAAAGGTTTGGGAAGGATTACAAGTAGCTTGGCTTGTAGTGGAA  
AAAAACGAGAGATTAACCATTTCCAAGCAGTTGCCCCAGAAGTTTTGCTGAACTGTTACAT  
CAGTGTGTTGGGAAGCTGATGCCAAGAAACGGCCATCATTCAAGCAAATCATTTCATCTG  
GAGTCCATGTCAAATGACACGAGCCTTCCTGACAAGTGTAACCTCATTCCTACACAACAAG  
GCGGAGTGGAGGTGCGAAATTGAGGCAACTCTTGAGAGGCTAAAGAAACTAGAGCGTGAT  
CTCAGCTTTAAGGAGCAGGAGCTTAAAGAACGAGAAAGACGTTTTAAAGATGTGGGAGCAA  
AAGCTGACAGAGCAGTCCAACACCCCCGCTGCTGCCTTCCTTTGAGATTGGTGCATGGACG  
GAAGACGATGTGTATTGGTGGGTTTCAGCAGCTCGTCAGAAAAGGTGACTCTTCAGCAGAG  
ATGAGTGTATATGCAAGCTTGTTTTAAAGAAAACAACATTACAGGGAAGCGGCTGCTGCTG  
CTGGAGGAAGAAGACCTGAAAGACATGGGCATTGTCTCCAAGGGGCATATCATTCACTTC  
AAGTCAGCCATTGAGAAATTAACCCATGATTACATAAATTTGTTTTCACTTCCCACCACTA  
ATTAAGGACTCAGGAGGTGAACCTGAAGAAAATGAGGAAAAAATAGTGAACCTGGAACCTG  
GTTTTTGGTTTTTCACTTGAAACCAGGAACTGGCCCCACAGGATTGTAAGTGGAAAATGTAT  
ATGGAGATGGATGGGGATGAAATTGCAATAACCTACATAAAAGATGTGACATTCAACACT  
AACCTACCTGATGCGGAGATTTTAAAGATGACAAAGCCACCATTGTGTAATGGAGAAGTGG  
ATTGTAGGAATAGCAAAAAGTCAGACTGTGGAGTGCCTGTACATATGAGAGTGATGTT  
AGAACTCCAAAAAGCACTAAACATGTCCATTTGATTCACTGGAGTAGAACAAAACCTCAG  
GATGAAGTGAAAGCAGTCCAACCTTGCCATTTCAGACATTATTCACCAATTCAGATGGCAAC  
CCTGGAAGCAGGTCCGACTCAAGTGCTGATTGCCAGTGGTTAGATACTCTGAGGATGCGG  
CAGATTGCATCCAACACTTCTTTACAGCGTTCCCAGAGCAATCCTATTCTGGGGTCACCG  
TTCTTCTCACACTTTGATGGCCAGGATTCCTACGCTGCTGCTGTGAGACGGCCCCAGGTG  
CCCATTAAAGTATCAACAGATTACACCTGTGAACCAGTCCAGAAGCTCGTCTCCTACTCAG  
TATGGACTGACCAAAAACCTTCTCTTCTTACATCTCAACTCTAGGGACAGTGGCTTTTCC  
AGTGGCAATACTGACACCTCTTCAGAGAGGGGTCGATACTCAGACAGAAGCAGGAACAAA  
TATGGACGTGGTAGTATATCACTCAATTCTTCTCCTAGAGGAAGATACAGTGGAAAGAGT  
CAGCATTCCACTCCATCAAGAGGAAGATACCCTGGAAAGTTCTACAGGGTTTCTCAGTCA  
GCACTCAATCCTCACCAGTCGCCTGACTTCAAGAGAAGCCCCAGGGACCTCCACCAACCC  
AACACCATAACCAGGGATGCCTTTGCACCCTGAGACTGACTCAAGAGCCAGTGAAGAGGAC  
AGCAAAGTCAGCGAAGGGGGCTGGACAAAAGTGGAATACCGGAAAAAGCCCCACAGGCCA  
TCTCCCGCCAAAACCAATAAAGAGAGAGCCAGAGGGGACCACCGTGGATGGAGAACTTT  
TGA

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ATGGGAAATTATAAATCTAGACCAACCCAAACTTGTACTGATGAATGGAAGAAAAAAGTC  
AGTGAATCATATGTTATCACAATAGAAAGATTAGAAGATGACCTGCAGATCAAGGAAAAA  
GAACTGACAGAACTAAGGAATATATTTGGCTCTGATGAAGCCTTCAGTAAAGTCAATTTA  
AATTACCGCACTGAAAATGGGCTGTCTCTACTTCATTTATGTTGCATTTGTGGAGGCAAG  
AAATCACATATTCGAACTCTTATGTTGAAAGGGCTCCGCCCATCTCGACTGACAAGAAAT  
GGATTTACAGCCTTGCATTTAGCAGTTTACAAGGATAATGCAGAATTGATCACTTCTCTG  
CTTCACAGTGGAGCTGATATACAGCAGGTTGGATACGGTGGCCTCACTGCCCTCCATATT  
GCTACAATAGCTGGCCACCTAGAGGCTGCTGATGTGCTGTTGCAACATGGAGCTAATGTC  
AATATTCAAGATGCAGTTTTTTTTCACTCCATTGCATATTGCAGCGTACTATGGACATGAA  
CAGGTAACCTCGCCTTCTTTTGAAATTTGGTGTGATGTAAATGTAAGTGGTGAAGTTGGA  
GATAGACCCCTCCACCTAGCATCTGCAAAAGGATTCTTGAATATTGCAAAACTCTTGATG  
GAAGAAGGCAGCAAAGCAGATGTGAATGCTCAAGATAATGAAGACCATGTCCCACCTCCAT  
TTCTGTTCTCGATTTGGACACCATGATATAGTTAAGTATCTGCTGCAAAGTGATTTGGAA  
GTTCAACCTCATGTTGTTAATATCTATGGAGATACCCCTTACACCTGGCATGCTACAAAT



## FIGURE 2000

GGCAAATTTGAAGTTGCCAAGGAAATCATCCAAATATCAGGAACAGAAAGTCTGACTAAG  
GAAAACATCTTCAGTGAAACAGCTTTTCATAGTGCTTGTACCTATGGCAAGAGCATTTGAC  
CTAGTCAAATTTCTTCTTGATCAGAATGTCATAAACATCAACCACCAAGGAAGGGATGGG  
CACACTGGATTACACTCTGCTTGCTACCACGGTCACATTCGCCTGGTTCAGTTCTTACTG  
GATAATGGAGCTGATATGAATCTAGTGGCTTGTGATCCCAGCAGGTCTAGTGGTGAAAAA  
GATGAGCAGACATGTTTGATGTGGGCTTATGAAAAAGGGCATGATGCCATTGTCACACTC  
CTGAAGCATTATAAGAGACCACAAGATGAATTGCCCTGTAATGAATATTCTCAGCCTGGA  
GGAGATGGCTCCTATGTGTCTGTTCCATCACCCCTTGGGGAAGATTAAAAGCATGACAAAA  
GAGAAGGCAGATATTCTCCTCCTAAGAGCTGGATTGCCTTCACATTTCCATCTTCAGCTC  
TCAGAAATTGAGTTCCATGAGATTATTGGCTCAGGTTCTTTTGGGAAAGTATATAAAGGA  
CGATGCAGAAATAAAATAGTGGCTATAAAACGTTATCGAGCCAATACCTACTGCTCCAAG  
TCAGATGTGGATATGTTTTGCCGAGAGGTGTCCATTCTCTGCCAGCTCAATCATCCCTGC  
GTAATTCAGTTTGTGGGTGCTTGCTTGAATGATCCCAGCCAGTTTGCCATTGTCACTCAA  
TACATATCAGGGGGTCTCTGTCTCCCTCCTTCATGAGCAGAAGAGGATTCTTGATTTG  
CAGTCTAAATTAATTATTGCAGTAGATGTTGCCAAAGGCATGGAGTACCTTCACAACCTG  
ACACAGCCAATTATACATCGTGACTTGAACAGTCACAATATTCTTCTCTATGAGGATGGG  
CATGCTGTGGTGGCAGATTTTGGAGAATCAAGATTTCTACAGTCTCTGGATGAAGACAAC  
ATGACAAAACAACCTGGGAACCTCCGTTGGATGGCTCCTGAGGTGTTACGCAGTGCACT  
CGGTACACCATCAAAGCAGATGTCTTCAGCTATGCTCTGTGTCTGTGGGAAATTCTCACT  
GGCGAAATTCCATTGCTCATCTCAAGCCAGCGGCTGCGGCAGCAGACATGGCTTACCAC  
CACATCAGACCTCCCATTTGGCTATTCCATTCCCAAGCCCATATCATCTCTGCTGATACGA  
GGGTGGAACGCATGTCCTGAAGGAAGACCCGAATTTTCTGAAGTTGTCATGAAGTTAGAA  
GAGTGTCTCTGCAACATTGAGCTGATGTCTCCTGCATCAAGTAACAGCAGTGGGTCTCTC  
TCACCTTCTTCTTCTTCTGATTGCCTGGTGAACCGGGGAGGACCTGGCCGGAGTCATGTG  
GCAGCATTAAAGAAGTCGTTTCGAATTGGAATATGCTCTAAATGCAAGGTCCTATGCTGCT  
TTGTCCCAAAGTGCTGGACAATATTCCTCTCAAGGTCTGTCTTTGGAGGAGATGAAAAGA  
AGTCTTCAATACACACCCATTGACAAATATGGCTATGTATCCGATCCCATGAGCTCAATG  
CATTTTCATTCTTGCCGAAATAGTAGCAGCTTTGAGGACAGCAGCTGA

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ATGATTTCTTGCCTGTNATAACCTATGCACTCACAAAGATGAACTCTCTGAGAGGGATGA  
GCAAGAGCTTCAGGAAATCCGAAAGTATTTCTCCTTTCTGTATTCTTTTTTCAAAGTGCC  
GAAACTGGGCTCGGAGATAATAGACTCCTCAACCAGGAGAATGGAGAGCGAAAGATCACC  
GCTTTATCGCCAGCTAATTGACCTGGGCTATCTGAGCAGCAGTCACTGGAACCTGTGGGGC  
TCCTGGCCAGGATACTAAAGCTCAGAGCATGTTGGTGGAACAGAGTGAAAAGCTGAGACA  
CTTGAGCACATTTTCTCACCAGGTGTTACAGACTCGCCTGGTGGATGCAGCCAAGGCCCT  
GAACCTGGTGCCTGCACTGCCCTTGACATCTTTATTAACCAGGCATTTGACATGCAGCG  
GGACCTGCAGATCACTCCCAAACGTCTGGAATATACTCGAAAAAAGGAGAATGAGTTGTA  
TGAATCATTGATGAATATTGCCAACCGAAAGCAGGAGGAAATGAAGGATATGATTGTTGA  
GACACTTAATACCATGAAGGAGGAACTTCTGGATGATGCTACTAACATGGAGTTTAAAGA  
CGTCATTGTCCCTGAGAATGGAGAACCAGTAGGCACCAGAGAGATCAAATGCTGCATCCG  
ACAGATCCAGGAACCTCATCATCTCCCGACTTAATCAGGCAGTGGCTAATAAGCTGATCAG  
CTCAGTGGATTACCTGAGGGAAAGCTTCGTGCGGAACCCTGGAACGATGTCTGCAGAGCCT  
GGAGAAGTCTCAGGATGTCTCAGTTCACATCACAGTAATTATCTCAAACAGATCTTAAA  
TGCTGCCTATCATGTTGAAGTCACGTTTCACTCAGGGTCGTGAGTTACAAGGATGCTATG  
GGAGCAAATCAAACAGATCATCCAGCGCATCACATGGGTGAGCCACCTGCCATCACTCT  
GGAATGGAAGAGGAAGGTGGCCCAGGAAGCCATTGAGAGCCTCAGCGCCTCCAAATTGGC  
TAAGAGCATTTGCAGCCAATTCCGGACTCGGCTCAATAGTTCCACAGAGGCTTTTGCAGC  
CTCCTTGCGGCAGCTGGAAGCTGGCCACTCAGGCCGGTTAGAGAAAACGGAAGATCTATG  
GCTGAGGGTTCCGAAAGATCATGCTCCCCGCCTGGCCCGCTTTCTCTGGAAAGCCGTTT

## FIGURE 2PPP

TTTACAGGATGTCTTGCTTCATCGTAAACCTAAACTGGGACAGGAACTGGGCGGGGGCCA  
GTATGGTGTGGTATACCTGTGTGACAACTGGGGAGGACACTTCCCTTGTGCCCTCAAATC  
AGTTGTCCCTCCAGATGAGAAGCACTGGAATGATCTGGCTTTGGAATTTCACTATATGAG  
GTCTCTGCCGAAGCATGAGCGATTGGTGGATCTCCATGGTTCAGTCATTGACTACAACTA  
TGGTGGTGGCTCCAGCATTGCTGTGCTCCTCATTATGGAGCGGCTACACCGGGATCTCTA  
CACAGGGCTGAAGGCTGGGCTGACCCTGGAGACACGTTTGCAGATAGCACTAGATGTGGT  
GGAGGGAATCCGCTTCCTGCACAGCCAGGGACTTGTCCATCGTGATATCAAACCTGAAAAA  
TGTGCTGCTGGATAAGCAGAACCGTGCCAAGATCACTGACTTAGGATTCTGCAAGCCAGA  
GGCCATGATGTCAGGCAGCATTGTGGGGACACCAATCCATATGGCCCCCTGAACTTTTCAC  
AGGGAAGTACGATAATTCCGTGGATGTCTACGCTTTTGGGAATTCTTTTCTGGTATATCTG  
CTCAGGCTCTGTCAAGCTCCCTGAGGCATTTGAGAGGTGTGCTAGCAAAGACCATCTCTG  
GAACAATGTGCGGAGGGGGGCTCGCCCAGAACGTCTTCCTGTGTTTGATGAGGAGTGCTG  
GCAGTTGATGGAAGCCTGTTGGGATGGCGACCCCTTGAAGAGGCCTCTCTTGGGCATTGT  
CCAGCCCATGCTCCAGGGCATCATGAATCGGCTCTGCAAGTCCAATTCTGAGCAGCCAAA  
CAGAGGACTAGATGATTCTACTTGAAAGCAAAGACCTTTCTCTTTCACTCTCTAGTTATT  
TCCTTCCCCCTCACCATTTGGCCATGGGGAGAATTTGACATTTATTCACTATAGGACACA  
CTCCCAAGGGAACCTGGTGCTTGCTGGGAAACTTGGAACCTTCCCAGGCAGGGATGACTCC  
TGGACAGTGAAGAGTTGAATGACTGAGCATATTCAGCAGCTCACTGAAGCGCCAAGCTAT  
CCCTTTAGCAAAAAAGTGTCTCAGATGTGTAAAGCTGAGGAATGTGGTGTCTGGCTTC  
ACAAATGAAAAGGAGGCAGATGTT

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TTGATGTCAACCTGAAGGCTTCTAAAGCGAGTGATGTCTACAGCTTTGGGATCCTCGTGT  
GGGCAGTGCTGGCTGGCAGAGAAGCTGAGTTGGTAGACAAGACTTCACTAATCCGGGAAA  
CAGTGTGTGACAGGCAGAGTCGTCCTCCACTGACAGAGCTGCCTCCAGGTAGCCCTGAGA  
CTCCCGGCTTGGAAAACTGAAGGAGTTAATGATTTCATTGCTGGGGTTCCCAGTCCGAAA  
ACAGGCCATCCTTCCAGGACTGCGAACCAAAAACCAATGAAGTTTACAATCTGGTAAAGG  
ACAAGGTAGATGCTGCTGTCTCCGAGGTAAAGCATTATCTGTCTCAGCACAGAAGCAGCG  
GCAGAAACTTGTCTGCCAGAGAGCCAAGCCAAAGAGGCACAGAAATGGATTGCCCCGAGGG  
AAACCATGGTTTCTAAAATGCTGGACCGCCTGCATTTGGAGGAACCCCTCCGGACCAGTTC  
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GGACATCTTCTGACCCCGTGGCTGGCACTCCTCAGATTCCACATACTTTACCCTTCAGAG  
GCACAACACCTGGGCCAGTCTTTACTGAGACTCCCGGTCTCACCCTCAAAGGAATCAGG  
GAGATGGAAGACACGGCACTCCTTGGTATCCCTGGACCCCAACGAATCCAATGACAGGGC  
CACCGGCTCTCGTCTTCAACAACCTGTTCTGAAGTGCAGATTGGGAACTACAACCTCCTTGG  
TAGCACCACCAAGAACTACTGCCTCAAGTTCGGCCAAGTATGACCAAGCACAGTTTCGGCA  
GGGGTAGGGGCTGGCAGCCCTTCCACAAGTAGACTTCAGAGAATCACTGCAAGAGCCTGA  
AGTGTGCCATTCAGCGTGGCAATAAAAAGCACGTTTTTAAGCAACCTGGACTGGCTAAGAC  
AGTCCTTGCCACTTCCTGAAGCTCACAACATTCTGTGAGGACAGTTGGACCTACACCCAA  
ACTGACTCTTGACCCATCTCCTTAAAGTCAATAAACATAGCATGTTAACTGTG

SEQ ID NO: 86\_AA744236\_H

ATGGGATCAGAGAACAGTGCTTTAAAGAGCTATACACTGAGAGAACCACCATTTACCTTA  
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GTGTATAAGAGAGAAAAATGAAGACAAGGTTAATAAAGCTGCCAAGCATTGGAAGACACTT  
CGTCACCCCTTGCTTGCTAAGATTTTTTATCTTGTACTGTGGAAGCGGATGGCATTTCATCTT  
GTCACTGAGCGAGTACAGCCCCCTGGAAGTGGCTTTGGAAACATTGTCTTCTGCAGAGCTC  
TGTGCTGGGATCTATGACATATTGCTGGCTCTTATCTTCCCTTCATGACAGAGGACACCTA  
ACACACAATAATGTCTGTTTATCATCTGTGTTTGTGAGTGAAGATGGACACTGGAAGCTA  
GGAGGAATGGAACTGTTTGTAAAGTTTCTCAGGCCACACCAGAGTTTCTGAGGAGTATT

## FIGURE 2QQQ

CAGTCAATAAGAGACCCAGCATCTATCCCTCCTGAAGAGATGTCTCCAGAATTCACAACCT  
CTCCCAGAGTGTTCATGGACATGCCCCGGGATGCCTTTTTCATTTGGAACATTGGTGGAAAGT  
TTGCTCACAATCTTAAATGAACAGGTTTCAGCGGATGTTCTCTCCAGCTTTCAACAGACC  
TTGCACTCAACTTTGCTGAATCCCATTCCAAAATGTCGGCCAGCGCTCTGCACCTTACTA  
TCTCATGACTTCTTCAGAAATGATTTTCTGGAAGTTGTGAATTTCTTGAAAAGTTTAACA  
TTGAAGAGTGAAGAGGAGAAAACGGAATTCTTTAAATTTCTGCTGGACAGAGTCAGCTGC  
TTGTCAGAGGAATTGATAGCTTCAAGGTTGGTGCCTCTTCTGCTTAATCAGTTGGTGT  
GCAGAGCCAGTGGCTGTTAAGAGTTTTCTTCCTTATCTGCTTGGCCCCAAAAAAGATCAT  
GCGCAGGGAGAACTCCTTGCTTGCTCTCACCAGCCCTGTTCCAGTCACGGGTGATCCCC  
GTGCTTCTCCAGTTGTTTGAAGTTCATGAAGAGCATGTGCGGATGGTGTCTGTCTCAC  
ATCGAGGCCTACGTGGAGCACTTCACTCAGGAGCAGCTGAAGAAAGTCATCTTGCCACAG  
GTTTTGCTGGGCCTGCGTGATACTAGCGATTCCATTGTGGCAATTACTCTGCATAGCCTA  
GCAGTGCTGGTCTCTCTGCTTGGACCAGAGGTGGTTGTGGGAGGAGAACGAACCAAGATC  
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TTTTCTCAGCCTATTAAATTTCCCATAAATGGACTCTCAGATGTAAAAAATACTTCGGAG  
GACAGTGAAAACCTCCCATCAAGTTCTAAAAAGTCTGAGGAGTGGCCTGACTGGAGTGAA  
CCTGAGGAGCCTGAAAATCAAACGTCAACATACAGATTTGGCCTAGAGAACCTTGATGAT  
GATGTCAAGTCCCAGTGCACCTTGGATGTGGAAGAGTCATCTTGGGATGACTGCGAG  
CCCAGCAGCTTAGATACTAAAGTAAACCCAGGAGGTGGAATCACTGCTACAAAACCTGTT  
ACCTCAGGGGAGCAGAAGCCTATTCTGCTTTGCTTTCACTCACTGAAGAGTCTATGCCT  
TGGAAATCAAGCTTACCCCAAAAGATTAGCCTTGTACAAAGGGGGGATGACGCAGACCAA  
ATCGAGCCGCCAAAAGTGTTCATCACAAGAAAGGCCCTTAAGGTTCCATCAGAACTTGGT  
TTAGGAGAGGAATTCACCATTCAAGTAAAAAAGAAGCCAGTAAAAGATCCTGAGATGGAT  
TGGTTTGCTGATATGATCCCAGAAATTAAGCCTTCTGCTGCTTTTCTTATATTACCTGAA  
CTGAGGACAGAAATGGTCCCCAAAAAAGGATGATGTCTCCCCAGTGATGCAGTTTTCTCA  
AAATTTGCTGCAGCAGAAATTACTGAGGGAGAGGCTGAAGGCTGGGAAGAAGAAGGGGAG  
CTGAACCTGGGAAGATAATAACTGGTGA

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AGCGGCCGCGGGGGCGGCGGAGGATATGGAGTAAAGCCAGAGTCAGTGGCCAGGCACGAA  
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CCGCCCCCTCCTGGAAGAAGGAAGAGGTAACCTATACTACCCAATATTGCAGCCATGGAGT  
CCATGCTTAATAAATTGAAGAGTACTGTTACAAAAGTCACAGCTGATGTCACCTAGTGCGG  
TAATGGGAATTCCTGTCACTAGAGAATTTGATGTTGGTCGACACATTGCCAGTGGTTGCA  
ATGGGCTAGCTTGGAAGATTTTTTAATGGCACAAAAAAGTCAACAAAGCAGGAAGTGGCAG  
TTTTTGCTTTTGATAAAAAAAGTATTGACAAGTATCAAAAATTTGAAAAGGATCAAATCA  
TTGATTCTCTAAAACGAGGAGTCCAACAGTTAACTCGGCTTCGACACCCTCGACTTCTTA  
CTGTCCAGCATCCTTTAGAAGAATCCAGGGATTGCTTGGCATTTTGTACAGAACCAGTTT  
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GGAAACCTATATTTGAAGTCAACAAGCAAGATATTTACAAGAGTTTCAGTAGGCAGTTGG  
ATCAGTTGAGTCGTTTAGGATCTAGTTCACTTACAAATATACCTGAGGAAGTTCGTGAAC  
ATGTAAAGCTACTGTAAATGTAAGTCCGACTGTAAGACCAGATGCAGATCAAATGACAA  
AGATTCCCTTCTTTGATGATGTTGGTGCAGTAACACTGCAATATTTTGATACCTTATTCC  
AAAGAGATAATCTTCAGAAATCACAGTTTTTCAAAGGACTGCCAAAGGTTCTACCAAAAC



## FIGURE 2RRR

TGCCCAAGCGTGTCATTGTGCAGAGAATTTTGCCTTGTTTGACTTCAGAATTTGTAAACC  
CTGACATGCTACCTTTTGTGTTTGGCCCAATGTTCTACTTATTGCTGAGGAATGCACCAAAG  
AAGAATATGTCAAATTAATTCTTCCTGAACTTGGCCCTGTGTTTAAAGCAGCAGGAGCCAA  
TCCAGATTTTGTAAATTTTCTACAAAAAATGGATTTGCTACTAACC AAAACCCCTCCTG  
ATGAGATAAAGAACAGTGTTCTACCCATGGTTTACAGAGCACTAGAAGCTCCTTCCATTG  
AGATCCAGGAGCTCTGTCTAAACATCATTCCAACCTTTGCAAATCTTATAGACTACCCAT  
CCATGAAAAACGCTTTGATACCAAGAATTAAAAATGCTTGCTACAAACATCTTCCCTTGC  
GGTTCGTGTAAATTCATTAAACAACATTGGAGCAGACCTTCTGACTGGCAGTGAGTCCG

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GGCGCGCCAGATATCACACGTGCCAAGGGGCTGGCTCAGCCCCGGCTCGGGCGGCGCGGAG  
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GGGACCCGGTCCGGGACTTTCCGTTCGAGCTCATCCCGGAGCCCCCAGAGGGCGGCCTGC  
CCGGGCCCCTGGGCCCCTGCACCGCGGCCGCAAGAAGGCCACAGGCAGCCCCGTGTCCATCT  
TCGTCTATGATGTGAAGCCTGGCGCGGAAGAGCAGACCCAGGTGGCCAAAGCTGCCTTCA  
AGCGCTTCAAAACTCTACGGCACCCCAACATCCTGGCTTACATCGATGGACTGGAGACAG  
AAAAATGCCTCCACGTCGTGACAGAGGCTGTGACCCCGTTGGGAATATACCTCAAGGCGA  
GAGTGGAGGCTGGTGGCCTGAAGGAGCTGGAGATCTCCTGGGGGCTACACCAGATCGTGA  
AAGCCCTCAGCTTCTTGGTCAACGACTGCAGCCTCATCCACAACAATGTCTGCATGGCCG  
CCGTGTTCTGTGGACCGAGCTGGCGAGTGGAAGCTTGGGGGCTTGGACTACATGTATTGCG  
CCCAGGGCAACGGTGGGGGACCTCCCCGCAAGGGGATCCCCGAGCTTGAGCAGTATGACC  
CCCCGGAGTTGGCTGACAGCAGTGGCAGAGTGGTCAGAGAGAAGTGGTCAGCAGACATGT  
GGCGCTTGGGCTGCCTCATTTGGGAAGTCTTCAATGGGGCCCCTACCTCGGGCAGCAGCCC  
TACGCAACCCTGGGAAGATCCCCAAAACGCTGGTGCCCCATTACTGTGAGCTGGTGGGAG  
CAAACCCCAAGGTGCGTCCCAACCCAGCCCGCTTCTTGCAGAACTGCCGGGCACCTGGTG  
GCTTCATGAGCAACCGCTTTGTAGAAACCAACCTCTTCTTGGAGGAGATTGAGATCAAAG  
AGCCAGCCGAGAAGCAAAAATTCTTCCAGGAGCTGAGCAAGAGCCTGGACGCATTTCCCTG  
AGGATTTCTGTGCGGCACAAGGTGCTGCCCCAGCTGCTGACCGCCTTCGAGTTCGGCAATG  
CTGGGGCCGTTGTCTCTACGCCCCCTCTTCAAGGTGGGCAAGTTCCTGAGCGCTGAGGAGT  
ATCAGCAGAAGATCATCCCTGTGGTGGTCAAGATGTTCTCATCCACTGACCGGGCCATGC  
GCATCCGCTCCTGCAGCAGATGGAGCAGTTCATCCAGTACCTTGACGAGCCAACAGTCA  
ACACCCAGATCTTCCCCCACGTCGTACATGGCTTCTTGGACACCAACCTGCCATCCGGG  
AGCAGACGGTCAAGTCCATGCTGCTCCTGGCCCCAAAGCTGAACGAGGCCAACCTCAATG  
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GCAACACCACAGTCTGCCTGGGCAAAATCGGCTCCTACCTCAGTGCTAGCACCAGACACA  
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TACTGCAAGGGCGGCTACCA<sup>-</sup>CCCTGTGAAGATCGGCGACGTGTTCAATGGGCGGTACCA  
GTGGTGCGCAA<sup>-</sup>ACTGGGCTGGGGCCACTTCTCCACCGTCTGGCTCTGCTGGGACATCCAG  
CGCAAGCGCTTTGTGGCCCTCAAAGTGGTGAAGAGTGCGGGGCATTACACGGAGACAGCT  
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## FIGURE 2TTT

TGCATGGTGCTGGAGGTGCTGGGGCCACCAGCTCCTCAAATGGATCATCAAGTCCAACTAC  
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AAGCTGTCCAAAAACAAGAGGAAGAAGATGAGGCGCAAACGGAAACAGCAGAAGCGGCTG  
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CTCAAGCACTGGGGCCTGTACGAGGTACTCATGGAAAAGTACGAGTGGCCCCCTAGAGCAG  
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SEQ ID NO: 91\_SGK022\_H

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AGCATGGAGGACTTTCTGCTCTCCAATGGGTACCAGCTGGGCAAGACCATTGGGGGAAGGG  
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SEQ ID NO: 92\_AA060026\_M SGK022\_M

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ACCGGGACCTTAAGTGTGAGAACGCCTTGTTGCAGGGCTTCAACCTGAAGCTGACCGACTT  
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## FIGURE 2VVV

CATCATGGTCTGCGGCTCCATGCCCTATGACGACTCCGACATCAGGAAGATGCTGCGTAT  
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CGACCACCGGCCCCGACCACAAGCTTGGAGCCAAAACCCAGCACCGGCTGCTGGTGGTGCC  
CGAGAACGAGAACAGGATGGAGGACAGGCTGGCCGAGACCTCCAGGGCCAAAGACCATCA  
CATCTCCGGAGCTGAGGTGGGGAAAGCAAGCACCTAGCATGACAATGGCCCCGTTGTGTG  
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TT

SEQ ID NO: 95\_AA883975\_H

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GCCCCATGGCTACCCAGACCTGAGCACCACTACTGCGGCTCAGCCGCCCTACGCGTCACCC  
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GTGCTCTACGTCATGGTCAACGGGTGCATGCCCTTCGACGACTCGGACATCGCCGGCCTG  
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SEQ ID NO: 96\_AA905446\_H

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## FIGURE 2WWW

SEQ ID NO: 97\_H29974\_H

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CCTGGGTTATGCTGAGGAGCCCTGCTATCTCTGGTTTGTTCATGGAGTTCTGTGAAGGTGG  
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AGAAAACCCAAAGATGGAGTTGCACATCCCCCAAAAACGCAGGACTTCCATGTCTGAGGG  
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SEQ ID NO: 98\_AA498104\_M H29974\_M

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GGCCGAGGTAGTTACGGTGTGTGTATGAAGCAGTCATCAGAAAGACCTCTGCACGGGTG  
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AAAGATAGCAGCTGGGAAACGTGACACATATTATTTGCAAATACCATGGATGATATGCTG  
CTTCTGTTTAAACAGTGATGCAACATTATGTGGCTGAAAAAGAATATAAAAAGCTAGACTC  
TACCCTCTAAGGGTTTAGATTTTTTTGTGGGATTTTTTTTTTTTCTCATTTTTCTTAAATCC  
AAGTTGGCCGTTTTTATTAGTATGTTTCAAATGTGTATTACCAATGTGGGTGTAAATTTTT  
AAAAAATGATTATTGATAGAAGTTTGGCAGGAAAATTCTTTAAGAGCTAACAAGAGAAGA  
GAGTCCAGTTTTTCTGGAAATATGTCTTTAAGTATTTTAGACATTCTCGTCAGTATTAGG  
AATTTCCATGGGAAAAGAGGTTTGCATGCTGGTAATGCAACCTTTGAACTTTGTAAAGG  
AAACATATATGTATATATTTATGTATATGTAAGTATGTGAATGTGCGCATTTTGCATTCC  
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TGCTGGTGAAGTCAGTGACGAAAAATAAACCTTCCCTTATCTTCCTACTCTGCCCCCTCCC  
CCTAATGAAATCATATTAAGTNGTTTTTCC'NNNTTTTTTTGTAAATATACAGCTTTTTTTTT  
TAAGGCATCATTTTTCGAGGGTCTAAAATTATCTGGTAAAACAAATGAAATTAAGTGATCC  
AAAGCTGCTGAAGTATGTTTGAAGCTCCAGTGCCCTATAGCTGCAAGAGTTGAATTAGT  
CATGCAGTCATATGGCAGCAGGTTGGTGATT

GCGGGGCTCCGTATCCCCACGTGGGGCCCTGCAGGAAGTGGGGGGGGCGCGTGACCCGGGG  
AGGCCCAGAGACAGGGGAGGGGGCGCCGGGAGCCGGGGCGGATCCGGGTCCCCGATGCGGGG  
TGCATTTCCGGCGGGGCGGGCGCTGGGGGCGAGCGTGGAGCCACCCAGTGTCTGGGCCCGGCC  
GCAACCCGGCCGGAACCGGCGCTCCGGCAGCGAGGAAGCGGCCCGCGCGGGGGCGCAGGCGGGCGG  
AATGGCGGGGGCCCCGGCTGGGGTCCCCCGCGCGCTGGACGGCTTCATCCTCACCGAGCGGCT  
GGGCAGCGGGCACGTACGCCACGGTGTACAAGGCCTACGCCAAGAAGGACACTCGTGAAGT

## FIGURE 2YYY

GGTAGCCATAAAGTGTGTAGCCAAGAAAAGTCTGAACAAGGCATCGGTGGAGAACCTCCT  
CACGGAGATTGAGATCCTCAAGGGCATTTCGACATCCCCACATTGTGCAGCTGAAAGACTT  
TCAGTGGGACAGTGACAATATCTACCTCATCATGGAGTTTTGCGCAGGGGGGCGACCTGTC  
TCGCTTCATCCATACCCGCGAGGATTCTGCCTGAGAAGGTGGCGCGTGTCTTCATGCAGCA  
ATTAGCTAGCGCCCTGCAATTCCTGCATGAACGGAATATCTCTCACCTGGATCTGAAGCC  
ACAGAACATTCTACTGAGCTCCTTGGAGAAGCCCCACCTAAACTGGCAGACTTTGGTTT  
CGCACAACACATGTCCCCGTGGGATGAGAAGCACGTGCTCCGTGGCTCCCCCCTCTACAT  
GGCCCCCGAGATGGTGTGCCAGCGGCAGTATGACGCCCGCGTGGACCTCTGGTCCATGGG  
GGTCATCCTGTATGAAGCCCTCTTCGGGCGAGCCCCCCTTTGCCTCCAGGTCGTTCTCGGA  
GCTGGAAGAGAAGATCCGTAGCAACCGGGTCATCGAGCTCCCCTTGCGGGCCCCCTGCTCTC  
CCGAGACTGCCGGGACCTACTGCAGCGGCTCCTGGAGCGGGACCCAGCCGTCGCATCTC  
CTTCCAGGACTTCTTTGCGCACCCCTGGGTGGACCTGGAGCACATGCCCAGTGGGGAGAG  
TCTGGGGCGAGCAACCGCCCTGGTGGTGCAGGCTGTGAAGAAAGACCAGGAGGGGGATTTC  
AGCAGCCGCTTATCACTCTACTGCAAGGCTCTGGACTTCTTTGTACCTGCCCTGCACTA  
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CTCTGCCCCGAGACCTGCTCAGAGAGATGGCCCCGGGACAAGCCACGCCTCCTAGCTGCCCT  
GGAAGTGGCTTCAGCTGCCATGGCCAAGGAGGAGGCCGCCGGCGGGGAGCAGGATGCCCT  
GGACCTGTACCAGCACAGCCTGGGGGAGCTACTGCTGTTGCTGCGGAGCCCCCGGGCCGG  
AGGCGGGAGCTGCTTCACACTGAGGTTCAAGAACCTCATGGCCCCGAGCTGAATACTTGAAG  
GAGCAGATGAGGGAATCTCGCTGGGAAGCTGACACCCTGGACAAAGAGGGACTGTCGGAA  
TCTGTTCTGTAGCTCTTGCACCCTTCAGTGACCCTAGAAGAATGATTGGACAGATGTGAGC  
CATCTGGAGCAGAGGGGGCACTAACCCAGGCTGACGCCAAGAATGAAGTGGCCCCACTGCAG  
CCCTGGCGAGCAGGCTTCTTGGATGGACAGTGCTGAGACCCCCATATCCCAGAGTCCCCA  
GCCTCCCTCAGGTTACTCTGCACCCACAGATGGTTTGATGGCTGTGCTGTATACTGGAG  
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TACTGGGTCTGTGCCTGTCCGTTTTTGGGGCATGCAGCCCTCTATCATTTTTTGGCTCCGA  
GAAGAGGGCAAGGGGGCCCCCGCAGGGTACTTCTGTGCTTGCCCTCGCCCTGCCAGCAGGC  
AGCTGTGCCCTGGCCTGCCCTTCCCGGGACCCCTTATTCCAACCTCAGCTCCTCTTTGCA  
CTGGAATGGGGCACTCCAACACCCCTCAGGGACCACCCCTCCCCACAGTATGCACTCAGCC  
CCACAGAACCCACCAGTCTTTCTGGGAACCTCACACCTGCCCGCCATCTTGGTACTTTAGG  
TTAATCCCTCAAGCATGAAAGCTGGATCTTTTGGGGTTTAAGAAGCCCAAGCCTTGTTCC  
TGCCCTGGCCTAGGGAGCACTCAGGAGGGTTCCTTGGTCCTCATCTCTCCACCTCCGTT  
CCCTCTGGGCCCCACACTAGCCACAGCGCGGGCCTTGTGCTGGAGTTTGAGCCTGGGACA  
GGGAGAGGGAGGCTTGGAGACAGTCTGACCCAGTGCCCTCTAGGCCACCCACTTCTAGGC  
CTGCCCTGCCGCCGTGGAGCCCTGGGCAAGCTCTTTCCTTTCTGGGCCTGGGTCTCCC  
CATCTCTTCAATGGGGCTGATACCTTCACAGCCCACAGCATGGGCACTTATGAGGACAAA  
GTGAATTTAACCCTGGAAAAGAATGTATTTGAGAGTTTCTTTTAAATAATCAGCGGGTGTT  
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GAAGTCGGCCCAGAGATGGAAAACCTTTATTCTGTATGAGGAGATCGGAAGAGGAAGCAAG  
ACTGTTGTCTATAAAGGGCGACGGAAGGGAACAATCAATTTTGTAGCCATTCTTTGTACT  
GATAAGTGCAGAAGGCCTGAAATAACCAACTGGGTCCGTCTCACCCGTGAAATAAAACAC  
AAGAATATTGTAACCTTTTCATGAATGGTATGAAACAAGCAACCACCTCTGGCTAGTGXAT  
GAAAACCTCCCAGAAGATGTTGTGAGAGAATTTGGAATTGACCTGATTAGTGGATTACAT  
CATCTTCATAAACTTGGCATTCTCTTTTGTGACATTTCTCCTAGGAAGATACTCTTGGAA



## FIGURE 2ZZZ

GGGCTGGCACA CTGAA GTTTAGCAACTTTTGCTTGGCAAAAGTGGAAGSTGAAAAATTTC  
GAAGAGTTCTTTGCTTTGGTGGCAGCAGAGGAAGGAGGAGGTGATAATGGGGAAAATGTC  
CTGAAGAAAAGCATGAAAAGTAGAGTCAAAGSATCTCCTGTATATACAGCACCAGAAAGTT  
GTGAGGGGTGCTGACTTTTCCATCTCCAGTGACCTCTGGTCTTTGGGCTGTCTGCTTTAT  
GAAATGTTTTTCAGGAAAACCTCCATTCTTCTCAGAAAGTGTTTCAGAATTAAGTGAAG  
ATCTTATGTGAAGATCCTTTGCCACCTATTCCGAAAGATTCTTCTCGTCTTAAAGCTTCT  
TCAGATTTTATTAATTTGCTTGATGGGTACTTCAAAGAGATCCTCAGAAAAGATTGACT  
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TCAAGCGTCGAAGATCTCAGTCTCAGCAGAAACACTATGGAGTGTTCTGGGCCACAAGAT  
TCCAAGGAGCTTTTGCAAGAACTCTCAGAGTAGACAAGCAAAGGGCACAAGAGTGGTCAA  
CCACTAGGTCACTCTTTCAGACTAGAAAATCCAAGTGAAGTTTCGGCCTAAGAGTACTCTT  
GAGGGTCAATTGAATGAATCCATGTTTCTTCTCAGTTCTCGTCTACTCCCAGAACTAGC  
ACTGCAGTGGAAGTAAGTCCTGGTGAGGATATGACTCACTGTTCAACACAGAAGACTTCT  
CCTCTGACCAAGATTACAAGTGGACACCTGAGTCAGCAGGACCTGGAATCCCAGATGAGA  
GAGCTTATCTACACGGACTCAGATCTTGTTGTCAACCCCATTTATCGACAATCCAAAGATA  
ATGAAACAGCCACCAGTTAAATTTGATGCAAAAATATTGCATCTACCAACATATTCAGTG  
GATAAGTTATTATTTCTGAAAGATCAAGATTGGAATGACTTTTTTGCAACAAGTGTGCTCG  
CAGATCGACTCCACTGAGAAGAGCATGGGGGGCTCCCGAGCCAAGCTGAATCTCCTTTGC  
TATTTGTGCGTGGTGGCTGGTCACCAGGAGGTGGCCACCAGGCTCCTCCATTCCCCCCTG  
TTCCAATTGCTAATCCAGCATTTGCGGATAGCTCCAAACTGGGATATACGGGCCAAGGTT  
GCTCACGTGATTGGTTTACTGGCTTCGCACACAAGTGAAGTCCAGGAAAATACACCTGTT  
GTTGAGACTACAAGCTCCATTGGAATCGGGATTTTGAAGTGTCTTGTTCAACACTCCACT  
CCAGTGCCTAGACAGTGCCTTGTGTATGTATAGATACTGACAAATATTTCAAATAAATA  
AAACTGTATCAGCATT

SEQ ID NO: 102\_SGK384\_H

TCTTTGGCCCACGTGCTGAGGGCGCGGCAGATCCTGACGGAGCCAGAAGTGCGCGACTAC  
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SEQ ID NO: 103\_AA210451\_M SGK384\_M

GGTCTGCTGCATGGATAATGGACTGGAACACAGAAAGACCATGCAGGGTTCGGCTGTAGA  
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GGTTGTGAGCTGCCATGTTGAACCAAGCAGGTCACTGAGGGACACAGGCATGTGGATGGA  
AACCTGCTGGGAGAAAAAAGAAACTGCTGAAGGGACTGACATGGGACAGCAACATGGAA  
CCAGGAATGGTCTCACGCATAGAGAGCTCCCCCGGGGCGTGGGGCTGCTGCTCGCCATGG  
CCCTTATGAACGTGGCGCTCTACCTCTGCCTTGATCAGCTTTTCATCTCCCCTGGACGAT  
CCACCGCGGACTCTAGGCGCTGTCTCCGGGCTACTTCAGAATGGGGCGGATGAGAAACT  
GCTCACGCTGGCTGTCTGTGAAGAGCTGAGGACAGAAGTCAGGCAGCTGAAGCGCGTTG  
GGGAGGGAGCCGTGAAGAGAGTCTTTCTGTCTGAATGGAAGGAACACAAAGTCGCTCTCT  
CCCGGCTCACAGGCTGGAGATGAAGGAGGACTTCCTGCATGGGCTGCAGATGCTGAAGT  
CTCTACAGAGTGAGCACGTGGTCACGCTGGTGGGCTACTGTGAGGAAGATGGCACTATTC  
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TCTCCAGTTTCTCTTGGGGCACGTGGAAGGGAGTGATATGGTTAGATTCCATTTGTTTG  
ATATCCATAAGGCGTGCAAGAGCCAGATCCCGGCAGAAAGACCCACTGCTCAGAACGTGC



## FIGURE 2AAAA

TAGACGCTTACCAGAGGGTTTTCCATTCACTCCGAGACACTGTGATGTCGCAGACGAAAG  
AAATGCTGTAAAAATGAGCCATCGAGTGACGTGCTTGATGGCTGAATGGCATCCCAGCTG  
TTCCGCTCTTGATGATGGAAGAGCTTTGCATGGATGGATGTTGACCCTGGCTGTTTCAGCC  
ACGTAGGCCTCCTCTACGTCTGCCTGCATGTTTGAGTGTTCTGCTCTCCTGGCAGCCCCG  
ATGGAAGCTGCCAAGCGAGAAAGCCTGGCTTCAGGATGCTCCCTGGTGAAGATGCAGAGG  
ATTCTGGATCTGCATAGTTTCAAGGGAGTGATCAAACGGTGACCTTGAAGACATGCTGCC  
TGCCTTGGTAACTTTTTTATAGACTAGTAGGAAACAGAAATCTTTTGGGGGAGGGGGGGAC  
AACCCTAGTTTCCTCAGAGACAATTTCTTCTCATTGAGAAAGCCCTGTTGGAAGCTGGG  
GATGTTTTTAACTCCGTGGCAGGGCACTTGCCTAGTTGTGTGCAAAGCCTTGGATCTGACC  
CATGGCATGTGCACACACACAAATGCTCAAAGAAAATCCCAGACGCCAGAAGTGTGCCCC  
TTTCTTGTCAATAAGGTCATTGTCAGTACCGGAGATGATTTTTTTTATGAAGCGTTTATG  
CTGACTCGTGTCACTGAGCCAAGTGTGCATGGTCGTTAGCTACTTTGTGGGTTCTTCTTT  
CTTTCTACCCTACTTCTTCCCTTTCCACCCCCCTAACACTAGATAGGAGAGAGGAGAGAGA  
AAGGAAAGTGGGCACTGTTATATTGTTGGACGACTTCTTGCTGATTAAGGGGTGTCGAGT  
TCCTTGGAGCAATGATCTTTGCTGCCAAGATATCTCATTTCTTCTTGTTCCTTCTTCGCC  
CACGACCCTTCACAAACACCGACCAACAGCAAACAACAACCCACCCCGCTTCTCGGGGG  
CCCTAGCACTTATGTACTTCTGAAAAGTCCCCAGAAATTCCAATCATCACACACTCAGAG  
AACTGTCTGCTGCTGGCAAACTACACCCCTGCTAGAGCATGAGGCAAATCATAGTCAG  
CTGCTGTGGACAGTCTGAAGCAGCCTGGCATCCCACACCTGAGATTAAACAAAAACATT  
CTTACCTGTGTTTTGTTTTTGTTTTAAGAAACCAAAGTGCACCAAGATAGCATGCTCTTG  
AGATTGTGGCTGTCTAGAGATTTTTTGGAACAGCAAGTTGAAGGAACTTTCTTACCTGCCT  
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GTCCCCCTGTACCGGAAAGTACAAAGTCTGCTCTGGGCTTGATGCCTGAACACTTTAAA  
ACACTGTGGAGCCAGGAATAATGGTACCCACCTGTAATCCCAGCACCTGGGAGACAGGAG  
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CAATAAAAAAACAAAAAGGTC

SEQ ID NO: 104\_SGK071\_2\_H

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AATGAGCTCAGCTTCCAGGAGGTCATTGAGGATAAGAGGAAGGCAAAGAAAATCATTGAC  
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GCCAAGGCTCCCTGCAACCAAGCCATCACCTCCACCCCTGCTGAGTGCTCTTCAGAGCCAC  
CCCGAGGAGGAGCCACTTCTTGTTCATGGTCTACAGCCTGCTAGCCATCACCAACAACCCAG

## FIGURE 2BBBB

GAGTCAGAGTCACTGTCAGAGGAGCTGCAGAACGCTGGGCTGCTGGAGCACATCCTGGAG  
CACCTCAACAGCTCCCTCGAAAGCAGGGACGTCTGCGCCAGCGGCTGGGCTGCTCTGG  
GCCCTCCTGCTGGACGACCCCATCTTGGCACTCCAGCGCCCCAGGAAAAAGAGAGCTCCA  
AACCACGGAAAGCCCCGGGAAACCCAAGAACCCTGCCAGCACCCAAAGTATCATTGTGAAC  
AAGGCCCCCTTGGAGAAGGTCCCGGACCTCATCAGCCAGGTGTTGGCCACCTACCCCTGGG  
GATGGGGAAATGGCAGAAGCCAGCTGCGGAGTCTTCTGGCTGCTGTCCCTGCTGGGCTGC  
ATCAAGGAGCAGCAGTTTGAACAAGTGGTGGCGCTGCTCCTGCAAAGCATCCGGCTGTGC  
CAGGACAGAGCCCTGCTGGTGAACAATGCCTACCGGGGACTGGCCAGCCTGGTGAAGGTG  
TCAGAGCTGGCGGCCTTCAAGGTGGTGGTGCAGGAGGAGGGCGGCAGTGGCCTCAGCCTC  
ATCAAGGAGACCTACCAGCTCCACAGGGACGACCCGGAGGTGGTGGAGAACGTGGGCATG  
CTGCTGGTCCACCTGGCTTCCCTATGAGGAGATCCTGCCGGAGCTGGTGTCCAGTAGTATG  
AAGGCCCTGCTCCAGGAGATCAAGGAGCGCTTCACCTCCAGCCTGGTGTGAGTGACAGCAGC  
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GGGGGACTGGAATAG

SEQ ID NO: 105\_AA118352\_M SGK071\_M

CAGAAGAAGACCCCTGCCAGAAGTCCTGGATGGCTCCTGAAGCTCTCAAATTCTCCTTCT  
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TGAAGCCCATCCTGAAAACCATGGAGGAGAAGCAAATCCCTGGTACAGATGTCTACTATT  
TGCTTCTGCCCTTCATGTTGCATATCAACCCCTCCGATCGACTGGCAATCAAGGATGTGA  
TGCAAGTCACCTTCATGAGCAACTCCTTCAAAGCTCCTCTGTTGCGCTGAATATGCAGC  
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GTTTGATCATCTCCTTCCTGATGGATACCTTGCGGAGCCATCCTAACTCTGAAAGGCTTG  
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GGGACATCTGCCTCTCTATCCTGAGCCTGCTCTGGTCCCTCCTGGTAGATGTTGTCACTG  
TGGACAAAGAGCCCTTGGAGCAGCTCTCTGGCATGGTCACCTGGGTGCTGGCTACTCATC  
CGGAGGACGTGGAAATAGCAGAGGCTGGCTGTGCGGTGCTCTGGCTGCTGTCCTTGTTGG  
GCTGCATAAAGGAGAGTCAGTTTGAGCAGGTGGTAGTGCTGCTCCTGAGAAGCATCCAGC  
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GCATCAAAGACCTAGTCCAGGTGATCCGGGGGCGCTTTACCTCCAGCCTGGAGCTGATTT  
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SEQ ID NO: 106\_018653.9\_H

GGCCGGGGTGGGGGCGCGGGGCATGCGCGCGGGCTGGGCAGGGGGCGGGGGGGCGCAGA  
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## FIGURE 2CCCC

CGCCTCCTTCCTGCTGGGCTCCGTCTCAACGTGCTCTTCGCTCCGGGTCCGAGCCTCCG  
AGGCCAGGCCAGTCCCCTGAGCCTTCGCCGGCCCCGGGTGCGGGCCGTCGCGGGGGCCGC  
GGGGAGCTGGCCCCGGCAGATCCGGGGCGCGCTACGAGGAGGTGCAGCGCTATTCCCGCGGG  
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GGGCCCCGGCCTGCCGCGCCCCCGGCCCCCTTGGGCCCCGGCCCCCTGTCCGACGGCGCCCCA  
GGCTGGCCCCCGGCTCCCCGGCCCAGGCTCCCCCGGGCCCCGGGCCCCGCGCCTGGGCTGCGCC  
GCGCTTCGCAACGTGTCCGGCGCGCAGTACATGGGCTCAGGCTACACCAAGGCCGTGTAC  
CGGGTCCGCCTGCCCGGCGGTGCCGCGGTGGCGCTCAAGGCGGTGGACTTTAGCGGCCAC  
GATCTGGGCAGCTGCGTGCGCGAGTTCGGGGTACGGAGGGGCTGCTATCGGGCTGGCGGGC  
CACAAGCTGCTTAAGGAGATGGTGCTGCTGGAGCGGCTGCGGCACCCCCAACGTGCTGCAG  
CTCTATGGCTACTGCTACCAGGACAGCGAGGACATCCCAGACACCCTGACCACCATCACG  
GAGCTGGGCGCCCCCTGTAGAAATGATCCAGCTGCTGCAAACCTTCCTGGGAGGATCGATT  
CGAATCTGCCTGAGCCTGGGCGCGCTCCTCCACCACCTGGCCCCACTCCCCACTGGGCTCC  
GTCACCTCTGCTGGACTTCCGCCCTCGGCAGTTTGTGCTGGTGGATGGGGAGCTCAAAGTG  
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CTCGAGTTTCCGGCCAGGAACCTTCACCCTGCCCTGCTCAGCCCAGGGCTGGTGCGAGGGC  
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CACAGTGCCCCGCCTTCACTGCGTCCTCTGCTGGACAGCATCGTCAACGCCACAGGAGAG  
CTCGCCTGGGGGGTGGACGAGACCCTGGCCCAGCTGGAGAAGGTGCTGCACCTGTACCGG  
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GACAGCACCATCCCCCAGGAAGACTACCGCTGCTGGCCATCCTACCACCACGGGAGCTGC  
CTCCTTTCAGTGTTCAACCTGGCTGAGGCTGTGGATGTCTGTGAGAGCCATGCCCAGTGT  
CGGGCCTTTGTGGTCACCAACCAGACCACCTGGACAGGTCGGCAGCTGGTCTTTTTTCAAG  
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AACATCCCAGACAGACAGATGTGACCAGGACAAACGTGCAATAATGCCAAATGTTAAAAT  
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TGGGGACAATCCATCGTGGAGTGTTCTCTCAGCTTAGGTCTGGACAGGAGACTTGGCGGG  
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AGACTGGGGTCAGGGAGCAGGTGTGGTTTGAGCCAGGACCTGGGGCGGGGGTGGGGCCGG  
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SEQ ID NO: 107\_AA396601\_M

CCACGCGTCCGGGCTGCGCCGCGCTCCGCAACGTGTCTGGCGCGCAGTACGTGGGCTCAG  
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GGCACCCCAACGTGCTGCAGCTCTATGGCTATTGCTACCAGGACAGTGAGGGCATCCCAG  
ACACGCTGACCACCATCACAGAGCTGGGTGCCCTGTGGAGATGATCCAGCTGTTGCAGA  
CTTCCTGGGAGGATCGATTCCGAATCTGCCTCAGCCTTGGGCGCCTCCTCCACCACCTGG  
CCCACTCCCCGCTGGGCTCGGTCAACCCTGCTTGACTTCCGCCCCCTCGGCAGTTTGTGCTAG  
TGAACGGGGAGCTGAAAGTGACAGACCTGGATGATGCCCGCGGTGGAAGAGACACCGTGCA



## FIGURE 2DDDD

CCAGCAGTGCCGACTGCACGCTAGAGTTTCCAGCCAGGAACTTCAGCCTGCCCTGCTCGG  
CCCAGGGCTGGTGGGAGGGCATGAATGAGAAACGGAACCTCTACAATGCCTACAGGTTCT  
TCTTCACATACCTCCTGCCACACAGTGCCCCGCCTTCCCTCCGACCTCTCCTGGATAGCA  
TCGTCAATGCCACGGGAGAGCTCGCCTGGGGGGTGGATGAGACCCTGGCCCAGCTGGAGA  
CAGCGCTACACTTGTTCCGAAGTGGGCAGTACCTGCAGAACTCTACAAGCAGCAGGGCTG  
AGTACCAGCGCATCCCGGACAGTGCCATCACACAGGAGGACTATCGCTGCTGGCCATCCT  
ATCACCACGGCGGCTGCCTCCTGTCCGTGTTCAACCTGGCTGAGGCTATAGATGTCTGTG  
AGAGCCATGCTCAGTGTCGTGCCTTTGTGGTCACCAACCAGACCACCTGGACAGGTCGGA  
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CCTCATTTGCTTTCAGTGAAAGCCAGGGAGCAGCCGAGCCAGGCTCCTCCCACCTCCTGG  
AGGCCAGGCTCCTCCCCCTCCTGGAGGCCAGGCTCCTCCCCCTCCTGGAGTTTGCGTACC  
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SEQ ID NO: 108\_VRK3\_H

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GACAGTTCTGAGTCTGAAGATACTCTGAGTTCCTCTGAGAGATCCAAAGGCTCCGGGAGC  
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AAGCGGAGCCGAGTGACCACCTCACTTGAAGCTTTGCCCCACAGGGACAGTGCTGACAGAC  
AAGAGTGGGCGACAGTGGAAGCTGAAGTCCTTCCAGACCAGGGACAACCAGGGCATTTCTC  
TATGAAGCTGCACCCACCTCCACCCTCACCTGTGACTCAGGACCACAGAAGCAAAAGTTC  
TCACTCAAACCTGGATGCCAAGGATGGGCGCTTGTTCAATGAGCAGAACTTCTTCCAGCGG  
GCCGCCAAGCCTCTGCAAGTCAACAAGTGGGAAGAAGCTGTACTCGACCCCACTGCTGGCC  
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TGGATCAGGCCCTCAGAGACCCTGCAGAAGTACCTGAAGGTGGTGTGATGGCCCTCACGTAT  
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## FIGURE 2EEEE

SEQ ID NO: 109\_S71575\_M VRK3\_M

CCATCCCCACCTGTATCGGCTTTGGCATTACCCAGGACAAGTACAGGTTCCCTAGTATTCC  
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TAACTAGGCAGAAGCAGAAGTATCTGGACAGCCCCGAGCGCCTCGTGGGACTGTGTGGCC  
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CATAGCTCCTAAAAGAATCCCTTGAATGTGCATTCTCACCGCTCCCTTAGGACATATGAA  
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SEQ ID NO: 110\_AA45427\_H

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CAGCCAGTTTTAATGGACTTGGGTTCATGAATCAAGCATGCATCCATGTGGAGGGCTCC  
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CATTCTTCAGCATTGCGGCAGCTCCTGAACTCGATGATGACCGTGGACCCGCATCAGCGT  
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CATACTACCCAAATCTGA

SEQ ID NO: 111\_H05721\_H

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CGGCTTGGGGGGCGGGGGCGGGCGGGGCTGTGTCCGCGGGGAGCGTCCAGGCTGGGG  
CGCAGGACCGGGCGCGGAGCCTCGCAGGGTGGGGCTCGGGCTCCCTAACCGTCTCCGCTT  
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## FIGURE 2FFFF

GGGGGCCCCCTGCCTTCCCCCTTGGCCATCAAGATGATGTGGAACATCTCGGCAGGTTCCCTC  
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ACTCTGAAGGTGAGAATATTTTGTGGGCAGGTATCAACATTGGGGGAAGAGATTTTCATGTC  
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SEQ ID NO: 112\_AI086865\_H

AATGAGATGGAGAAGTACGAGCGGATCCGAGTGGTGGGGAGAGGTGCCTTCGGGATTGTG  
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## FIGURE 2HHHH

ACTGTCTGTGTGACTGATGAGGGTCAGCTCTATGCCTTCGGATCAGATTATTATGGCTGC  
ATGGGGGTGGACAAAGTTGCTGGCCCTGAAGTGCTAGAAACCCATGCAGCTGAACTTCTTC  
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GAGGATTATTATACACCACAAAAGGTGGATGTTCCCAAGGCCTTGATTATTGTTGCAGTT  
CAATGTGGCTGTGATGGGACATTTCTGTTGACCCAGTCAGGCAAAGTGCTGGCCTGTGGA  
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GCATACCATGAAGTTCCCTACACAACGTCCTTTACCTTGGCCAAACAGTTGTCCTTTTAT  
AAGATCCGTACCATTGCCCCAGGCAAGACTCACACAGCTGCTATTGATGAGCGAGGCCGG  
CTGCTGACCTTTGGCTGCAACAAGTGTGGGCAGCTGGGCGTTGGGAACCTACAAGAAGCGT  
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GGTGATGAGTTTACCATTGCTGCCACTGATGAGAAAGTATTGAATTCTAAGACCATCCGT  
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GGCGGGGGCGGCGGTGGTGAAGAAGAGGACAGTCAGCAGGAATCTGAAACTCCTGACCCA  
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TCTGAAGCTCCTTTGGAACACAAACCCCAAGTAGAAGCCTCGGTAACTGAGCTTTTGGCC  
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SEQ ID NO: 114\_R86668\_H, MKK6\_H

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## FIGURE 2III

ATCATTGACCAGGGCCACGCGGGTATGGGAAAGCAGCTGACATCTGGTCACTGGGCTGC  
ACTGTCATTGAGATGGCCACAGGTGCGCCCCCCTTCCACGAGCTCGGGAGCCCACAGGCT  
GCCATGTTTCAGGTGGGTATGTACAAGGTCCATCCGCCAATGCCCAGCTCTCTGTGCGGCC  
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GCGGCCGAGGAGCCTGCGTCTCCGGAGGAGAGTTCCGGGGCTGAGCCTGCTGCACCAGGAG  
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GAAATCCTGGCGGGGAAGGAACGGGAGTACCAGGCCCTGGTGCAGCGGGCTCTACAGCGG  
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SEQ ID NO: 115\_PAK6\_H

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ACCTTGTAACCATCACCCCTCCCTGCAGAGCAGTTCGCAGTACATCTCCACGGCTTCCTAC  
CTGAGCTCCCTCAGCCTCTCATCCAGCACCTACCCGCGCGCCAGCTGGGGCTCCTCCTCC  
GACCAGCAGCCCTCCAGGGTGTCCCATGAACAGTTTTCGGGCGGGCCCTGCAGCTGGTGGTC  
AGCCCAGGAGACCCAGGGAATACTTGGCCAACCTTTATCAAAATCGGGGAAGGCTCAACC  
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## FIGURE 2JJJ

GACCTCCGGAAGCAACAGAGACGAGAACTGCTTTTCAATGAGGTGCTGATCATGCGGGAT  
TACCACCATGACAATGTGGTTGACATGTACAGCAGCTACCTTGTCGGCGATGAGCTCTGG  
GTGGTCATGGAGTTTCTAGAAGGTGGTGCCTTGACAGACATTGTGACTCACACCAGAATG  
AATGAAGAACAGATAGCTACTGTCTGCCTGTCAGTTCTGAGAGCTCTCTCCTACCTTCAT  
AACCAAGGAGTGATTACAGGGACATAAAAAGTGACTCCATCCTCCTGACAAGCGATGGC  
CGGATAAAGTTGTCTGATTTTGGTTTCTGTGCTCAAGTTTCCAAAGAGGTGCCGAAGAGG  
AAATCATTGGTTGGCACTCCCTACTGGATGGCCCTGAGGTGATTTCTAGGCTACCTTAT  
GGGACAGAGGTGGACATCTGGTCCCTCGGGATCATGGTGATAGAAATGATTGATGGCGAG  
CCCCCTACTTCAATGAGCCTCCCTCCAGGCGATGCGGAGGATCCGGGACAGTTTACCT  
CCAAGAGTGAAGGACCTACACAAGGTTTCTTCAGTGCTCCGGGGATTCTTAGACTTGATG  
TTGGTGAGGGAGCCCTCTCAGAGAGCAACAGCCCAGGAACTCCTCGGACATCCATTCTTA  
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ATCGTCCCAACTTTGTTGGTTACTATCTTCCTCATCCTTCTTGGGGTCATCCTGTGGCTT  
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AGTTCTTCAGTCCTGAGCCCTACATGTGGGGCTGGAGGAGAACTATAACGGGAAAACCTC  
TGAGTTTCACTTAGGTATAGATAAAAGAAAGATGGTCCCCCTTTTATCTGATTCTGAGAC  
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## FIGURE 2KKKK

GAACATTCAACATGTATTGTTTCATTAAGCTAGCTTCCTAGTTCCGATTAGACTAAGGAGA  
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SEQ ID NO: 117\_AA098024\_M

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CAGAGAAAGAAAATCATGAAGAGACCCAGCAGCTGCTCACATGCCATGTACAACATCATG  
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CTAGAAGCTGCTTCTAGATCTGCCGATGACAAGGCTGTGTTGCAAGTGCCAGAGTTGGTG  
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SEQ ID NO: 118\_SGK2ALPHA\_H

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CCCACGGACTTCGACTTCCTCAAAGTCATCGGCAAGGGGAACCTACGGGAAGGTCTACTG  
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TTAAAGAAGAAAGAGCAGAGCCACATCATGGCAGAGCGEAGTGTGCTTCTGAAGAACGTG  
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## FIGURE 2LLLL

TCCACATTCTGTGGTACCCCTGAGTACTTGGCACCTGAAGTGCTTCGGAAAGAGCCTTAT  
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TTCAGCCCCATAAACTGGGATGACCTGTACCACAAGAGGCTAACTCCACCCTTCAACCCA  
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GTTGGGTAGGCAGCCAGCCCTCTTTTACCATAGGGCCTCCTGGTGTGTTGGATTTTGATCT  
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SEQ ID NO: 120\_CCRK\_H

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SEQ ID NO: 121\_TESK2\_H

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## FIGURE 2MMMM

CCCACCGCCTCCGCAGGCTAAGGAGCCGCTGCCACCAACGAGCTGTGAGGGTTACTATGC  
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AGTCAGTGTTACAGGT

